

The association of age-related cataract and serum Vitamin C

Yogish S. Kamath^{1,*}, Shailaja S. Bhat², Sameer Iqbal³, Lavanya G. Rao⁴

¹Associate Professor, ²Assistant Professor, Kasturba Medical College, Manipal University, ³Fellowship Resident, Ahalia foundation Eye Hospital, Palakkad, Kerala, ⁴Professor, Dept. of Ophthalmology, Srinivas Institute of Medical Sciences & Research Centre, Mukka, Mangaluru

***Corresponding Author:**

Email: dryogishkamath@yahoo.co.in

Abstract

Purpose: To study the association of age-related cataract with serum vitamin C levels in patients presenting to a University hospital in South India.

Materials and Methods: All patients above the age of 50 years, willing to participate in the study, were divided into two groups depending on the presence or absence of significant cataract. The serum Vitamin C levels of all participants were analyzed using the colorimetric technique, and any association between it and the type of cataract was studied.

Result: A total of 131 participants in each group were studied. The patients with denser cataracts had a significantly lower level of serum Vitamin C. (0.91 + - 0.40 mg dL in Group 1 with cataract versus 1.16 + 0.50 in Group 2 without minimal cataract. P value of 0.001). The low serum vitamin c levels were strongly associated with nuclear and cortical cataracts, but not with posterior subcapsular cataracts.

Conclusion: The etiology of age-related cataract is multifactorial. We attempt to highlight one of the modifiable parameters which may delay the progress of this condition.

Keywords: Cortical cataract; Nuclear cataract; Posterior subcapsular cataract; Senile cataract; Serum vitamin C

Introduction

Lens opacification accounts for blindness in 18 million and visual impairment in over 80 million people. This amounts to about one-half of the blindness and one-third of the visual impairment worldwide.⁽¹⁾ The morbidity from cataract disease is enormous, contributing to its status as a significant global public health burden. Around 4 million new cases of cataract are reported annually in India.⁽²⁾

Although there have been no satisfying explanations for the etiology of cataract formation, some studies have hinted that changes in the biochemical parameters that could lead to cataract formation. Several studies done to prove whether antioxidants, including serum vitamin C and E levels, could affect the rate of cataractogenesis, have shown mixed results with some studies proving a significant inverse association between age-related cataract and serum vitamin C levels.

We aimed to study the relationship between age-related cataract and serum vitamin C level by comparing the serum vitamin C levels between those patients with and without cataract and to analyze if the mean difference in serum vitamin C levels in these two groups is statistically significant.

Materials and Methods

The study was conducted at a tertiary care multispecialty university hospital in south India. The institute Ethical committee approval was obtained, and the study conducted as per the tenets of the Declaration of Helsinki. The duration of the study was from November 2013 to August 2015. All patients above 50 years of age visiting the outpatient clinic of the

department who agreed to participate in the study were included. After obtaining a written informed consent, a brief history of their ophthalmic complaints, systemic health, medication and surgery details were obtained. The participants then underwent assessment of visual acuity, slit lamp biomicroscopic evaluation of the anterior segment, intraocular pressure assessment with the Goldman applanation tonometer, followed by pupillary dilation with Tropicamide 1% eye drops. The lens opacity was then graded using the Lens Opacification Classification System III (LOCSIII). The examination of the posterior segment was carried out next, using indirect ophthalmoscopy.

The patients receiving any form of systemic or topical steroids were excluded from the study. Those with congenital cataracts, history of ocular trauma, significant intraocular infections including keratitis or previous ocular surgery were also excluded. Patients who had received significant electrical burns or radiation therapy were excluded.

All participants satisfying the above criteria were then subject to a blood sample analysis for vitamin C levels. This was measured at the biochemistry laboratory of the hospital using colorimetric technique using 2, 4 DNP.

The participants were divided into two cohorts, named Group 1 and Group 2, on the basis of the presence or absence of significant cataract respectively. As minimal lenticular opacification is expected with the advancing age, subjects with minimal opacities i.e. < Nuclear Opalescence 4 (NO4), Nuclear Color 4 (NC4) for nuclear cataract, <C 3 for cortical cataract and <P 2

for posterior subcapsular cataract were included in Group 2.

Results

A total of 131 consecutive participants, within the study period, were included in each group.

Gender distribution was almost equal to both the groups with Group 1 having 69 males and 62 females (total 131) and in Group 2, 67 were males and 64 were females. Age was normally distributed in subjects with a mean of 60.79 and standard deviation of 6.92. Other comorbidities like diabetes mellitus, ischemic heart disease, and bronchial asthma were evenly distributed in both groups with hypertension slightly more in Group 1.

In Group 1, significant nuclear cataract was present in 103 subjects, cortical cataract in 52 and posterior subcapsular cataract in 74 subjects.

The normal vitamin C levels in general population are found to be 0.6-2.00 mg/dl.(3,4) In both the Groups, vitamin C levels tended to be at the lower side. In 50% of subjects in Group 1, serum vitamin C levels were distributed between 0.61 – 1.16 mg/dl. In Group 2, it was between 0.77 – 1.39 mg/dl.

Statistical Analysis: Parametric values between the two groups were compared using Independent t-test. Non-parametric values were compared using Chi-square test. Correlation between serum vitamin C and types of cataract was established using Spearman's correlation. Outcomes of serum levels of vitamin C and type of cataract were analyzed using logistic regression.

On comparing the parameters between the two groups, (Table 1), the gender and systemic diseases associated were comparable, except for Hypertension which seemed more prevalent in Group 1 (p value < 0.05).

The serum levels of vitamin C were significantly lower among Group 1 (with significant cataract) than in Group 2 (with nil to minimal cataract); (p-value < 0.05).

Table 1: Comparison of various parameters between the Groups

| Parameters | Group 1% (n=131) | Group 2% (n=131) | p-value |
|------------------------|------------------|------------------|---------|
| Male | 53 (69) | 49 (65) | 0.535 |
| Diabetes mellitus | 34 (44) | 27(35) | 0.196 |
| Hypertension | 52 (67) | 32(42) | 0.001 |
| Ischemic Heart Disease | 7 (9) | 8(10) | 0.839 |
| Bronchial Asthma | 11 (14) | 6(8) | 0.169 |
| Vitamin C | 0.91 + 0.40 | 1.16 + 0.50 | <0.001 |

On comparing the similar parameters with the levels of vitamin C in the serum, (Table 2) no statistical difference was noted. However low serum vitamin C levels were associated with nuclear and cortical

cataracts, which was found to be statistically higher when compared to normal vitamin C group. (Both p-values < 0.05).

Table 2: Comparison of parameters with serum levels of vitamin C

| Parameters | Low vitamin C % (n=40) | Normal vitamin C % (n=222) | P value |
|---------------------------------|------------------------|----------------------------|---------|
| Age | 63.10 + 7.29 | 60.38 + 6.79 | 0.013 |
| Male | 53 (21) | 51 (113) | 0.852 |
| Diabetes mellitus | 38 (15) | 29 (64) | 0.271 |
| Hypertension | 50 (20) | 60 (133) | 0.242 |
| Ischemic Heart Disease | 3 (1) | 8 (18) | 0.208 |
| Bronchial Asthma | 10 (4) | 8 (18) | 0.691 |
| Nuclear Cataract | 58 (23) | 36 (80) | 0.011 |
| Cortical Cataract | 33 (13) | 18 (39) | 0.029 |
| Posterior Sub capsular Cataract | 33 (13) | 28 (61) | 0.516 |

(The normal vitamin C levels in general population are found to be **0.6-2.00** mg/dL. Level below 0.6 mg/dl is considered to be low.)

On attempting to establish a correlation between serum vitamin C levels and the type of cataract, using Spearman's rank correlation coefficient, an inverse relationship was established.(Table 3)

Both Nuclear and Cortical cataracts showed a strong negative correlation with serum levels of vitamin C which were statistically significant ($P_N = -0.27$ and $P_C = -0.194$ respectively with both p-values < 0.05).

Although a strong negative correlation between posterior subcapsular cataract and serum levels of vitamin C was obtained ($P_P = -0.085$), it was statistically not significant (p= 0.173).

Table 3: Correlation of the type of cataract and serum vitamin C level

| Type of cataract | P (Spearman's rank correlation coefficient) | P value |
|---------------------------------|---|---------|
| Nuclear cataract | - 0.27 | <0.001 |
| Cortical cataract | -0.194 | 0.002 |
| Posterior Sub capsular Cataract | -0.085 | 0.173 |

On applying logistic regression analysis to our data, we found, that in patients with low serum levels of vitamin C, there was a two-time higher risk of developing nuclear cataract than patients with normal vitamin C {2.4(95% CI 1.21 to 4.76; p=0.012} and a

two-time higher risk of developing cortical cataract than patients with normal vitamin C {2.2(95% CI 1.07 to 4.76; $p < 0.001$ }. However, low level of vitamin C was not an independent predictor for the development of posterior subcapsular cataract. (Table 4)

Table 4: Odds Ratio of type of cataract and vitamin C levels in serum

| | Reference | OR 95% CI | p-value |
|--|-------------------------|-----------------|---------|
| 1. Nuclear cataract | | | |
| Low vitamin C levels | Normal vitamin C levels | 2.4 (1.21-4.76) | 0.012* |
| 2. Cortical cataract | | | |
| Low vitamin C levels | Normal vitamin C levels | 2.2 (1.07-4.76) | < 0.001 |
| 3. Posterior Subcapsular cataract | | | |
| Low vitamin C levels | Normal vitamin C levels | 1.2 (0.61-2.62) | 0.51 |

(OR- Odds ratio CI- Confidence Interval * statistically significant)

Discussion

The association of vitamin C and eye disease has been discussed in various studies. Some randomized trials have found that the risk of development of cataract was unaffected by oral supplementation of multivitamins including vitamin C.⁽⁵⁾ A population based cohort study from Sweden, even found an increased risk of cataract development with the use of high dose supplements of vitamins E and C.⁽⁶⁾

However, other large population based studies have found an inverse association between age related cataract and vitamin C.^(7,8)

Our study aimed to find whether a significant difference exists between serum vitamin C levels in cataract patients when compared with normal individuals.

Amongst our study population, there was no significant difference between the serum vitamin C levels in males and females contrary to the study results conducted by S. Miratashi and Besharati which showed plasma levels of vitamin C were significantly higher in the female population.⁽⁹⁾

As our study had adopted the methodology of enrolling consecutive subjects meeting the selection criteria, age matching of the subjects in both groups was not done. Hence although the mean age in the Group 1 was 62.60 years and in Group 2 was 62.73 years, statistical analysis showed a difference which we did not consider clinically significant. However, studies with age-matched groups may have more statistically

accurate results than ours, and we consider the lack of age matching, a drawback in our methodology.

Other parameters including diabetes mellitus, bronchial asthma, and ischemic heart disease were comparable in both groups, implying serum vitamin C level is not significantly affected by them.

We found that plasma vitamin C level in our study population was on the lower side of normal range which was consistent with the findings of Ravindran et al and Dherani M et al. in Indian population.^(7,8) Despite an overall lower level of vitamin C in the serum in our cohorts, the odds ratio revealed a significant decrease in chance of cataract at levels above 0.6mg/dl compared with levels below this cut-off.

On comparing the means of the serum vitamin C levels between subjects of the Groups 1 and 2, a significant difference was noted ($p < 0.05$). These were consistent with the results of a cross-sectional (INDEYE feasibility) study carried out in a North Indian population in 2003.⁽⁸⁾

Amongst the subgroups, the cases with only nuclear cataract and with nuclear plus cortical cataract were the ones which showed statistically lower levels of serum vitamin C. The third subgroup with only posterior subcapsular cataract did not show a significant difference. But the in the study by Ravindran et al, posterior subcapsular cataract showed a stronger association with serum vitamin C levels.⁽⁷⁾ A recent meta-analysis carried out by Wei L, Liang G found out an inverse association between nuclear cataract, posterior subcapsular cataract and serum vitamin C levels. They concluded that higher vitamin C intake and serum ascorbate might decrease the risk of cataract.⁽¹⁰⁾

In the present study, the mean of serum vitamin C in group 1 with significant age-related cataract was 0.92 mg/dl versus 1.16 mg/dl of the other group, which declared a meaningful difference ($P < 0.05$). Though the mean of serum vitamin C of the subjects with significant cataract was in the normal range(0.6-2.00 mg/dl), it tended to be on the lower side of normal, and in comparison with group 2, the serum vitamin C levels of the patients were reduced. This indicates a significant inverse association between serum vitamin C level and cataract. These results were in favor of the studies by Ravindran and Dherani M et al. conducted in Indian population.^(7,8) Another study in Mediterranean east coast of Spain demonstrated that levels above 49 $\mu\text{mol/L}$ (0.86mg/dL) of ascorbic acid were significantly associated with a 64% reduced odds of cataract.⁽¹¹⁾

The results of our study give considerable supportive evidence for the association between decreased serum vitamin C level and senile cataract, largely confirming earlier such studies. Though aging by itself is the most important risk factor for cataract formation, other factors such as a family history of cataract and oxidative stress due to free radical generation may also play an intervening role. Multiple studies have been done to clarify the relationship

between antioxidants like vitamin C or E and cataract formation. Most of the studies compared the relation of senile cataract with vitamin C or E intake rather than the association of serum levels.

To conclude our study provides considerable evidence that serum vitamin C could be a protective factor against nuclear and cortical cataract formation which in turn is probably affected by oral intake of vitamin C. Hence further studies may be warranted in Indian population for determining a minimum level of serum vitamin C which could aid us in formulating a dose of dietary supplementation which would delay the process of formation of visually significant cataract.

Contributors

All the authors contributed to the design of the study. SI carried out the study including consents. YSK and SI have contributed to the manuscript preparation.

Ethics approval

The study was approved by the Institutional Ethical committee.

References

1. "Visual impairment and blindness Fact Sheet N°282". August 2014. <http://www.who.int/mediacentre/factsheets/fs282/en>. Retrieved 23 May 2015.
2. Minassian DC, Mehra V. Blinded by cataract: Each year projection from the first epidemiological study of the incidence of cataract blindness in India. *British Journal of Ophthalmology* 1990;74:341-343.
3. Vitamin C. Available at <http://www.vitamin-basics.com/index?id=43>. Accessed: April 18, 2012.
4. Kumar V. Robbins and Cotran Pathologic Basis of Disease, Professional Edition. 8th. Saunders; 2009:437-438.
5. William G. Christen, ScD, Robert J. Glynn: Age-related Cataract in a Randomized Trial of Vitamins E and C in Men; *Arch Ophthalmol* 2010 November;128(11):1397–1405.
6. Jinjin Zheng Selin, Susanne Rautiainen: High-Dose Supplements of Vitamins C and E, Low-Dose Multivitamins, and the Risk of Age-related Cataract: A Population-based Prospective Cohort Study of Men. *Am J Epidemiol* 2013;177(6):548–555.
7. Ravindran RD, Vashist P, Gupta SK. Inverse association of vitamin C with cataract in older people in India. *Ophthalmology* 2011 Oct;118(10):1958-1965.
8. Dherani M, Murthy GV, Gupta SK. Blood levels of vitamin C, carotenoids and retinol are inversely associated with cataract in a North Indian population. *Invest Ophthalmol Vis Sci* 2008 Aug;49(8):3328-35.
9. Miratashi SM, Besharati MR, Shoja MR, et al. Evaluation of vitamin C concentration of aqueous humor in senile cataract. *Medical Journal of Islamic Academy of Sciences* 2001;14(1):35–40.
10. Wei L, Liang G, Cai C, Lv J.: Association of vitamin C with the risk of age-related cataract: a meta-analysis. *Acta Ophthalmol* 2016 May;94(3):e170-6. doi: 10.1111/aos.12688
11. Valero MP, Fletcher AE, De Stavola BL. Vitamin C is associated with reduced risk of cataract in a Mediterranean population. *J. Nutr* 2002;132:1299–1306.