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Research Article

Association between Low Serum Vitamin C Level and Cataract in Elderly Patients

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Abstract

Background: Cataract is a vision impairing disease characterized by gradual, progressive opacification of the lens. Oxidative agents like ultraviolet (UV) rays are one of the most important causes of cataract. Antioxidant vitamins, in particular vitamin C can play a role in preventing the onset or progression of age related cataract.

Aim of Study: The aim of this study is to determine the correlation between low serum vitamin C and age related cataract.

Subjects and Methods: The study was carried out on 100 subjects. Fifty patients with cataract attending the out-patient department at Ibn - Alhaitham teaching eye hospital in Baghdad were compared with age matched fifty healthy volunteers. Serum vitamin C level was measured by ELISA technique.

Results: The mean Serum Vitamin C level in Cataract patients was (0.47 ± 0.38) and (0.81 ± 0.52) mg/dl in controls. Vitamin C level in the test group was significantly lower than the control group (P. value = 0.001). No statistically significant correlation had been found between vitamin C levels and age, sex and location of residency in all comparisons (P > 0.05). The low serum vitamin c levels were strongly associated with mature and nuclear cataracts.

Conclusion: This study revealed that serum vitamin C level in senile cataract patients was lower than normal individuals but its association with age, gender, residency in cataractous patients was statistically insignificant. Mature and nuclear cataract were associated with more significant decrease in serum vitamin C level than other types of cataract.

Keywords: *Vitamin C; Cataract*

Introduction

A cataract is a clouding of the natural intraocular crystalline lens that focuses the light entering the eye onto the retina. Age-related (or senile) cataract is defined as cataract occurring in people more than 50 years of age, unrelated to known mechanical, chemical, or radiation trauma [1].

Cataract is the leading cause of vision loss in the world. The World Health Organization (WHO) has estimated that 18 million people are bilaterally blind due to cataract and that the condition causes 48% of cases of blindness worldwide [2]. It is important to note that most cases of blindness due to cataract (up to 90%) are found in developing nations [3].

Cataracts may be congenital, metabolic, age related, or traumatic in origin. Because of their high prevalence, age related cataracts are presumed to have the greatest socioeconomic impact [3]. Senile cataract can be classified into 3 main types: nuclear cataract, cortical cataract, and posterior subcapsular cataract [4,5].

The pathophysiology behind senile cataracts is complex and yet to be fully understood. In all probability, its pathogenesis is multifactorial involving complex interactions between various physiologic processes modulated by environmental, genetic, nutritional, and systemic factors. As the lens ages, its weight and thickness increases while its accommodative power decreases. As the new cortical layers are added in a concentric pattern, the central nucleus is compressed and hardened in a process called nuclear sclerosis [6]. Chemical modification and proteolytic cleavage of crystalline (lens proteins) result in the formation of high-molecular-mass protein aggregates, these aggregates may become large enough to cause abrupt fluctuations in the local refractive index of the lens, thereby scattering light and reducing transparency. In addition, chemical modification of lens nuclear proteins also increases opacity, such that the lens becomes increasingly yellow or brown with advancing age. Other age-related changes include decreased concentrations of glutathione and potassium and increased concentrations of sodium and calcium in the lens cell cytoplasm [5].

Some of the following factors may provoke the above mechanisms for cataract. Oxidative stress - oxygen-free radicals (Oxidants) [7], Dyslipidemia [8], Smoking [9], Hypertension [10], Diabetes [11] and dehydrational crisis [12].

Vitamin C

Vitamin C, also known as ascorbic acid, is a water-soluble vitamin [13] cannot be produced by humans but is readily available in many types of food, Citrus fruits and vegetables [14] are the best known sources of Vitamin C. The Recommended Dietary Allowance (RDA) of vitamin C (measured in milligrams per day) is 90 mg/day for men and 75 mg/day for women [15]. The reference range of vitamin C level in serum is 0.6-2 mg/dl (Vitamin C) below this range vitamin C level consider as insufficiency [16].

Vitamin C is metabolized in the liver and excreted by the kidney. The renal threshold for excretion of vitamin C is 1.4 mg/100 ml. Excess vitamin C is excreted unchanged in the urine. When plasma concentrations of vitamin C are low, excretion of vitamin C is decreased [17]. Because of its capacity as a powerful free-radical fighter it is recommended in cases of many eye conditions, including senile cataract, macular degeneration, glaucoma and vitreous detachment [18-20]. It also helps to reduce corneal opacity caused by infectious keratitis [21].

The role of vitamin c in scavenging of free radicals in lens

Ocular tissues contain antioxidants that prevent damage from excessive oxygen metabolites: antioxidant enzymes, proteins, ascorbic acid, glutathione, amino acids (cysteine and tyrosine), uric acid, and others [22]. The fact that the incidence of cataract is higher in the population that is more exposed to sunlight imposes the assumption that photocatalytic conversion of molecular oxygen from ground state to excited states, which are highly reactive (superoxide anion ($O_2^{\bullet -}$), hydrogen peroxide (H_2O_2), hydroxyl radical ($OH^{\bullet}$), and others), occurs. However, despite the possibility of continuous production of these reactive molecular species in the aqueous humour and lens due to the continuous penetration of sunlight during the visual process, a latent period of development of cataract is long [23].

The role of ascorbate is important, as an effective scavenger of hydroxyl and superoxide anion radical. High concentration of ascorbate in the aqueous humour is assumed to represent a kind of filter that prevents the penetration of UV light in the lens and thus protects tissue from oxidative damage, particularly photo-induced damage [24].

It is assumed that vitamin C is transported into the aqueous humour in an oxidized form as dehydroascorbic acid and then converted to a reduced form, by the effect of dehydroascorbate reductase in the presence of reduced glutathione (GSH) mainly in the lens [24].

Vitamin C in the ocular structures function through ascorbate- dehydroascorbate redox system, which contributes to maintenance of reduced forms of pyridine nucleotides and maintenance of reduced glutathione. In the lens, the ascorbic acid prevents cation pumps damage induced by UV radiation and reduces photoperoxidation in the membranes [25].

Tripeptide glutathione is present in high concentration in the lens, mainly in reduced form (GSH) [26]. Glutathione together with ascorbic acid in the lens has many functions: it protects thiol groups of lens proteins against oxidation agents, it is necessary for the function of glutathione-peroxidase (which neutralizes reactive oxygen species), it is involved in detoxification of hydrophobic substances in

reactions catalysed by glutathione S-transferase enzymes. Proteins containing thiol groups are important for normal function of the lens epithelium, that is, enzyme Na-K-ATP-ase which affect cell permeability [27].

Aim of Study

The aim of this study is to determine the serum vitamin C levels in patients with senile cataract in comparison with age matched normal individuals.

Subjects and Methods

Study design

This study is a hospital-based, case-control study conducted between October 2017 and February 2018.

Subjects

The study included 100 subjects all of them were above 50 years of age (range 52 - 82 years).

Fifty patients with cataract attended outpatient department at Ibn- Alhaitham teaching eye hospital in Baghdad. They were selected on the basis of clinical history and examination. Questionnaire forms contained age, gender, occupation and residency (urban or rural). They were compared with 50 volunteers healthy subjects selected among hospital staff and patient' relatives.

Exclusion criteria: Subjects are excluded who are

- Diabetic
- receiving any form of systemic or topical steroids.
- Taking Vitamin C dietary Supplements.
- Subjected to significant electrical burns or radiation therapy
- With history of ocular trauma.
- With significant intraocular inflammation including uveitis, keratitis.
- With previous intraocular surgery.
- Heavy smokers.

Method of collection of data

All subjects underwent ophthalmic examination in form of visual acuity, refraction, slit lamp biomicroscopic evaluation of the anterior segment, intraocular pressure measurement with air puff tonometer, followed by dilatation of pupil with Tropicamide 1% eye drops, and cataract was classified according to its location as nuclear, cortical and posterior subcapsular cataract and according to maturity into mature and immature one. Examination of the posterior segment was finally done, using slitlamp biomicroscopy with 78 D condensing lens.

Five ml of blood sample was collected from each subject from a suitable peripheral vein (preferably antecubital vein) by venipuncture using a sterile disposable syringe. Blood samples then centrifuged and serum vitamin c level was measured by ELISA technique (The competitive enzyme immunoassay technique utilizing a monoclonal anti-VC antibody).

Statistical analysis

Data of the studied groups were entered, managed and analyzed using the statistical package for social sciences (SPSS) version 25 for windows. Descriptive statistics presented as frequencies, proportions, means and standard deviation (SD), and ranges. Statistical tests and analysis were performed according to the type of variables, chi square test used to assess the significance of association in cross-tabulation model, (categorical variables), Fisher's exact test was used as an alternative when Chi square was inapplicable (more than 20% of the cells in a table had expected values < 5). Student's t test (two independent groups) used to compare two means; multinomial logistic regression test was used to assess the estimate of risk of developing each type of cataract (odds ratio). Level of significance, (P-value) of

0.05 or less indicated significant difference, correlation or risk. Results and findings were presented in tables and figures with interpretation of the findings using the Microsoft Office Word Software version 2010.

Ethical issues

The study design and data collection were done after getting approval of Iraqi committee for medical specialization. All patients were informed about methodology and purpose of study and verbal consents of patients were obtained.

Results

There were 50 cataract patients and 50 controls enrolled in this study with a mean age of (64.6 ± 7.9) and (63.2 ± 6.8) years respectively as shown in table 1. Also, further distribution of the age into 10-year age intervals is shown in the same table. Both studied groups were almost matched for gender where 30 males and 20 females in cataract patients group and 31 males and 19 females in controls. Among cataract patients, 32 (64%) of urban residence compared 35 (70%) among controls, the remaining participants in both groups were of rural origin. The comparison of both studied group revealed no statistically significant difference in demographic variables, in all comparisons, P.value > 0.05 (Table 1).

		Cataract patient (n = 50)		Control (n = 50)		P value
Variable		No.	%	No.	%	
Age (year)	51 - 60	17	34.0	21	42.0	0.73
	61 - 70	23	46.0	21	42.0	
	> 70	10	20.0	8	16.0	
	mean ± SD*	64.6 ± 7.9	-	63.2 ± 6.8	-	0.38
Gender	Male	30	60.0	31	62.0	0.84
	Female	20	40.0	19	38.0	
Residency	Urban	32	64.0	35	70.0	0.52
	Rural	18	36.0	15	30.0	

Table 1: *Demographic characteristics of the studied groups.*
SD: Standard Deviation.

The Comparison of Serum Vitamin C level between the studied group revealed that Cataract patient had significantly lower serum vitamin C levels compared to controls; (0.47 ± 0.38) and (0.81 ± 0.52) mg/dl, respectively, (P. value was significant = 0.001) (Table 2).

	Serum Vitamin C level (mg/dl)	
	Cataract patient (n = 50)	Control (n = 50)
Mean ± SD	0.47 ± 0.38	0.81 ± 0.52
Minimum	0.12	0.12
Maximum	1.69	2.70
P value (comparison of means) = 0.001		

Table 2: *Comparison of serum vitamin C level of cataract patients and controls.*
SD: Standard Deviation.

The distribution of serum vitamin C level of both studied groups according to the standard reference values revealed that 36 (72%) cataract patients and 22 controls had low vitamin C levels, and 14 patients and 28 controls had normal vitamin C levels, which revealed

that cataract patients were more than 3 folds more likely to have low vitamin C levels compared to normal population (controls), (odds ratio 3.27, P. value 0.005) (Table 3).

	Cataract patient (n = 50)		Control (n = 50)	
Vitamin C level	**No.**	**%**	**No.**	**%**
Low	36	72.0	22	44.0
Normal	14	28.0	28	56.0
P value = 0.005 (significant)				

Table 3: *Distribution of serum vitamin C level of Cataract patients and controls according to reference values.*

Regarding the types of cataract, as it shown in figure 1, nuclear cataract was the more frequent type reported among cataract patients, it contributes for 60% of all types, followed by posterior subcapsular (22%), cortical (10%) and then mature cataract in (8%).

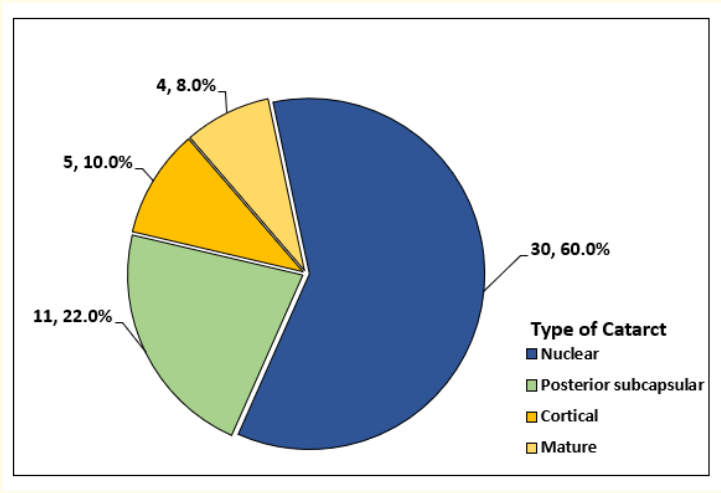

Figure 1: *Distribution of cataract patients according to the type of cataract.*

Further analysis was performed to assess the relationship between vitamin C levels from one side and the demographic variables and types of cataract from the other side in table 4, no statistically significant correlation had been found between vitamin C levels and demographic variables, (P > 0.05), in all comparisons. It had been significantly found that the lower vitamin C levels were in patients with mature cataract, followed by those with nuclear type, while patients with posterior subcapsular and cortical had higher levels, (P = 0.002). Moreover, as it shown in table 5, revealed that patients with low vitamin C levels had almost 6.5 folds (OR = 6.50, (P = 0.012) risk to have nuclear cataract than patients with normal vitamin C levels, on other hand those patients with posterior subcapsular and cortical cataract are less likely to have low vitamin C levels (OR = 0.22, 0.07 and p value = 0.026, 0.027 respectively).

Discussion

Cataract is an important visual problem of older people and a substantial health care cost in developing countries like Iraq. According to hospital - based study conducted at Ibn Al-Haitham Teaching Eye Hospital by Faiz I Ashakarchi cataract was the major cause of blindness in Iraq [28].

Variable	Statistic	Serum Vitamin C level		Total	P value
		Low (n = 36)	Normal (n = 14)		
Age (year)	Mean ± SD	65.5 ± 7.9	61.9 ± 7.4	-	0.14
Gender	Male n (%)	22 (73.3)	8 (26.7)	30	0.79
	Female n (%)	14 (70.0)	6 (30.0)	20	
Residency	Urban n (%)	21 (65.6)	11 (34.4)	32	0.31
	Rural n (%)	15 (83.3)	3 (16.7)	18	

Table 4: *Relationship between serum vitamin C levels and demographic characteristics of cataract patients (N = 50).*

Type of cataract	Serum vitamin C levels		Total	Odds ratio (95% CI)	P Value
	Low	Normal			
Nuclear	26	4	30	6.50 (1.65 - 25.58)	0.012 Significant
Posterior subcapsular	5	6	11	0.22 (0.05 - 0.89)	0.026 Significant
Cortical	1	4	5	0.07 (0.01 - 0.71)	0.027 significant
Mature	4	0	4	NA	-
Total	36	14	50		

Table 5: *Odds ratio of low serum vitamin C levels according to the types of cataract.*

Many risk factors are known to cause senile cataract and the most important preventable factors are ultraviolet (UV) rays especially UV-B rays exposure and nutritional deficiencies [29]. At present, the only remedy is surgical removal of the cataractous lens and substituting it with a lens made of synthetic polymers However, the incidence is so large that the available surgical facilities are unable to cope up with the problem. In addition to these, postoperative complications can occur such as posterior capsular opacification, endophthalmitis and uncorrected residual refractive error, Therefore, there is a search for pharmacological intervention that will maintain the transparency of the lens [30].

During the last decades, extensive research inputs have been made to delineate the etiology of cataract. Efforts have been directed to delay the onset and slow down the progression of cataract by various agents especially antioxidants like vitamin C. However, the potential role of vitamins in preventing cataract is well documented especially vitamin C which plays an important part in lens biology, both as an antioxidant and as a UV filter [31].

In this study, we tried to assess the relationship between vitamin C deficiency and senile cataract, hence, 50 patients with senile cataract were compared to 50 healthy controls and their serum vitamin C level. Patients and controls were compared regarding their age, gender and residence, and no statistically significant differences had been reported between both groups in these variables ($P > 0.05$), this comparisons in these variables were performed to exclude any possible confounding effect on the results, where vitamin C level could potentially affected by age, gender or residence, this indicated a good designing of the case control study. Many previous studies suggested an inter-correlation between cataract and these variables and also an inter-correlation between vitamin C levels and these variables [29,30,32].

In this study, Cataractous patients had significantly lower serum vitamin C levels compared to controls, the mean vitamin C level was (0.47 ± 0.38) and (0.81 ± 0.52) mg/dL, respectively, (P. value was significant = 0.001), this finding was also reported in Indian case control study conducted by Jaskiran Kaur., *et al.* [30], concluded that vitamin C concentration in patients with age related cataract was signifi-

cantly lower than control group (p value < 0.001), The result is so harmonic with our study. Several epidemiological studies have shown similar results of low serum vitamin C level in patients with senile cataract [32-34].

The results of our study give considerable supportive evidence for the association between decreased serum vitamin C level and senile cataract, strongly confirming earlier studies. The results appear to be important from the point of view of using this nutrient for delaying the onset of cataract development in human beings therapeutically as well as nutritionally

On the other hand, a recent Iranian case-control cross _sectional study performed by Mohammad Abbaszadeh., *et al.* [35], did not find a statistically significant association between senile cataract and serum vitamin C level.

This may be explained by two possibilities:

1. This study were included Iranian population whom dietary habit, socioeconomic state, UV-B rays exposure differ from our population; and this may be resulted in these differences.
2. The large samples of this study in comparison with ours may decrease the total bias of the outcomes.

Our study further analyze the correlation between vitamin C levels and other variables including the gender, residency and age of the cataractous patients and found no statistically significant differences in the frequency of vitamin C levels across these variables. No significant differences between both genders and between urban and rural patients and relatively lower vitamin C level in older age group, but it was statistically insignificant (p value = 0.14), on other hand. Other studies performed by Miratashi SM., *et al.* and Jalal D., *et al.* [29,32] concluded that vitamin C level was significantly lower in older age group, these inverse association between vitamin C level and age could be explained by decrease consumption of vitamin C rich food by elderly subjects, furthermore, these studies also revealed that vitamin C level is much lower in males compared to females and in urban compared to rural residents. However, the insignificant differences reported in the current study could be attributed to the small sample size in our study compared to these studies.

Regarding subtypes of cataract, nuclear cataract was the more frequent type reported among cataract patients, it contributes for 60% of all types, followed by posterior subcapsular (22%), cortical (10%) and then mature cataract in (8%). Further analysis to assess the correlation between subtypes of cataract and serum vitamin C level, revealed that the patient with low vitamin C level had almost 6.5 folds (Odd ratio = 6.5, p value = 0.012) risk to have nuclear cataract than the patients with normal vitamin C levels while those with posterior subcapsular and cortical cataract found to be less likely to have low serum vitamin C level (odd ratio = 0.22, 0.07, p value = 0.026, 0.027) respectively. Regarding mature cataract all patients had low serum vitamin C level (mean serum vitamin C = 0.196 mg/dl). The study shows significantly decreased levels of vitamin C in all morphological types of cataract which may be due to its utilization by counteracting ROS or due to its oxidation by O^{2-}.

Yogish S Kamath., *et al.* [36] found that only nuclear cataract had statistically lower levels of serum vitamin C. while those with posterior subcapsular and cortical cataract did not show a significant difference.

In the study performed by Ravindran., *et al.* [37], the posterior subcapsular cataract showed a stronger association with decrease serum vitamin C levels.

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 might decrease the risk of cataract [38].

The difference in correlation of vitamin C with the type of cataract across different studies may be attributed to differences in socioeconomic status of the communities and variable sample size.

To the best of our knowledge, this is the first study in Iraq regarding the association of vitamin C and age -related cataract. Although it has certain limitations including small sample size, lack of data on participants lifetime diets, their daily exposure time to sunlight, dietary vitamin C and aqueous humor concentration.

Conclusion

This study revealed that serum vitamin C level in senile cataract patients was lower than normal individuals but its association with age, gender, residency in cataractous patients was statistically insignificant. Patients with nuclear cataract had more significant decrease in serum vitamin C level than other types of cataract.

Recommendation

- Although the study showed significantly low vitamin C levels only in nuclear cataract, the intake of vitamin C rich food and supplements should be encouraged by elderly population. Popularization of its beneficial effects through educational and social instructions on the nutritional status of our diet can prevent or delay the initiation of cataract in developing countries like Iraq.
- Furthermore, Prospective studies of longer duration and with larger sample sizes are needed to clarify further the association between this vitamin and the development of senile cataract.

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