

DEFICIENCY OF VITAMIN C IN SOUTH ASIA

Rabia Mahmood Khan¹, M. Perwaiz Iqbal²

SUMMARY

Vitamin C (L-ascorbic acid) is a water soluble vitamin which is an antioxidant and has a wide variety of biological functions for growth and development of the human body. It is essential for maintaining good health. The objective of this review is to share with the scientific community, the status of vitamin C in the South Asian populations compared to other populations in the world. The focus in this review is on populations from Pakistan, India, Thailand, Malaysia, Nepal and Singapore.

Mean plasma levels of vitamin C of Indians/South Asians living abroad did not vary much compared to other ethnic groups, however, there was a significant decrease in these levels among those living in Pakistan and India. In general, males, smokers, persons using drugs of abuse, individuals infected with *H. pylori* or parasitic infections and those with low-HDL cholesterol have lower plasma levels of vitamin C when compared to females, non-smokers and normal healthy subjects free from drugs of abuse and infections (parasitic as well as *H. pylori*) and having normal levels of HDL cholesterol. In winter, plasma levels of vitamin C are, generally, higher compared to summer. Availability of non-sweet fruits, namely oranges, grape fruit, guava, lime and strawberries in winter could be the reason for that. There is a positive relationship between serum haptoglobin (Hp) levels and serum vitamin C concentrations. Individuals carrying a Hp2-2 phenotype (less stable Hp) have lower levels of vitamin C.

The prevalence of vitamin C deficiency (plasma levels < 2 µg/ml) is highest among Indians and people of South Asian origin compared to other races except the Mexican population. Lower intake of fresh fruits and vegetables and over-cooking of food by South Asians might contribute to the high prevalence of vitamin C deficiency in these populations. The high proportion of individuals with low levels of vitamin C in Pakistani, Indian, Malay and Chinese populations compared to most Western populations might explain higher rates of cardiovascular disease and cancer among South Asians.

KEY WORDS: Deficiency of vitamin C, L-Ascorbic acid, India, Pakistan, South Asians.

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1. Dr. Rabia Mahmood Khan
 2. Dr. M. Perwaiz Iqbal
- 1&2: Department of Biological & Biomedical Sciences
Aga Khan University,
Stadium Road,
Karachi.

Correspondence:

Dr. Mohammad Perwaiz Iqbal,
Professor of Biochemistry,
Department of Biological & Biomedical Sciences,
Aga Khan University,
Stadium Road,
P.O. Box-3500,
Karachi-74800.
E-Mail: perwaiz.iqbal@aku.edu

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INTRODUCTION

Vitamin C deficiency is not an exotic disease limited to ancient mariners. It is well reported in the elderly, alcoholics, mentally ill and food-faddists.¹ Probably the oldest reference to scurvy (the disease resulting from complete deprivation from exogenous ascorbic acid)² has been documented in Vasco da Gama's first journey to India (1497-1499).³ During the past 14 years, there have been relatively few studies conducted on the prevalence of vitamin C deficiency. The objective of this review is to find out the extent of the problem of vitamin C deficiency in South Asian populations compared

to other populations, and to emphasize the need to focus on the prevalence of vitamin C deficiency in Pakistani population and the strategies to be adopted to overcome this micronutrient's deficiency in our population.

Vitamin C and its biological functions: Vitamin C (L-ascorbic acid and its congener L-dehydroascorbic acid) is a white crystalline compound classified as a carbohydrate, with a molecular weight of 176. It is readily soluble in water and relatively stable in air. In aqueous solutions, however, ascorbic acid is attacked by oxygen and other oxidizing agents that convert the reduced form of the vitamin first to dehydroascorbic acid and then to further oxidation products in irreversible reactions. It is synthesized from glucose in the liver of most mammalian species, but not in humans, non-human primates and guinea pigs. This is because these species lack the enzyme gluconolactone oxidase, which is essential for the synthesis of ascorbic acid.⁴

Vitamin C is an electron donor and therefore a reducing agent. It is called an antioxidant because, by donating its electrons, it prevents other compounds from getting oxidized.⁴ It is required to build and maintain bone matrix, cartilage, dentine, collagen and connective tissue.⁵ It is involved in osteoblast proliferation, differentiation and function. In this regard, one of the roles of ascorbic acid is to keep iron in the reduced state (ferrous iron) which is required, together with oxygen molecule for the hydroxylation of the collagen molecule and hence the formation of bone matrix.⁶ It is necessary for folic acid absorption and for the regulation of the respiratory cycle in mitochondria and microsomes. It enhances the absorption of iron from the gastrointestinal tract via reduction of the ferric form to the more rapidly absorbable ferrous form.⁷ In the formation of hemoglobin and the maturation of red cells, it has a role in the removal of iron from ferritin, particularly in the reticuloendothelial cells of the liver, spleen, and bone marrow.

Animal studies have shown that ascorbic acid is necessary for the differentiation of

lymphoid organs during the growth of cockerels and young rats,⁸ and it enhances the regeneration of lymphoid tissue after X-irradiation.⁹ Ascorbic acid enhances the phagocytic action of leukocytes and the migratory behavior of neutrophils, thus, playing a role in the immune response of the body. Several other metabolic reactions require vitamin C as a cofactor. These include the synthesis of epinephrine from tyrosine and the synthesis of the bile acids. It is also believed that vitamin C is involved in the process of steroidogenesis since the adrenal cortex contains high levels of vitamin C which are depleted upon adrenocorticotrophic hormone (ACTH) stimulation of the gland.¹⁰ It is required in carbohydrate metabolism and in the synthesis of lipids and proteins. *Status of vitamin C in South East Asian populations:* The South East Asian region covered in this review includes: Pakistan, India, Thailand, Malaysia, Nepal and Singapore. During the past 14 years, there have been relatively few studies conducted on the prevalence of vitamin C deficiency, especially in this region. Tables-I, II and III summarize the results of these studies in terms of serum ascorbic acid levels and the prevalence of vitamin C deficiency among South Asians and other ethnic groups.¹¹⁻²⁴

Serum vitamin C levels were categorized according to internationally established limits: deficiency (less than 11 μ mol/l or < 2 μ g/ml), depletion (11-28 μ mol/l or 2-5 μ g/ml), and acceptable (more than 28 μ mol/l or >5 μ g/ml).^{20,21}

Effect of gender on vitamin C: From the data collected from various studies, it was observed that irrespective of age and ethnicity, the males show lower vitamin C levels compared to the females (Tables-I & II) and, therefore, a greater percentage of males would be having vitamin C deficiency (Table-III). For example, in the study by Hughes et al.¹⁴, the prevalence of vitamin C deficiency was significantly more among Indian males, Malay males and Chinese males compared to the female population in these ethnic groups (Table-III). Similarly, Chiplonkar et al.¹¹ have also reported 20%

Table-I: Comparison of serum ascorbic acid levels of South Asian males and females

Area, Country	Study Population	Age (Years)	Serum Ascorbic Acid Levels ($\mu\text{g/ml}$)				Study Group & Reference
			Males		Females		
			n	Mean \pm SD	n	Mean \pm SD	
Pune, India	Indians	20-50	214	3.0 \pm 1.2	108	3.5 \pm 1.2	Chiplonkar et al. (2002) ¹¹
Singapore	Indians	30-69	166	5.7	166	6.9	Hughes et al. (1998) ¹⁴
	Chinese		158	6.3	165	8.4	
	Malays		144	5.1	142	6.4	
United Kingdom	South Asian origin	40-59	168	5.8 \pm 0.26	160	6.56 \pm 0.32	Ness et al. (1999) ¹⁵
	African origin		140	6.42 \pm 0.28	215	8.09 \pm 0.25	
	Whites		147	6.83 \pm 0.28	188	9.22 \pm 0.28	
Lahore, Pakistan	Pakistanis	40-55	52	Hypertensive 2.86 \pm 1.20	31	Normotensive 5.4 \pm 0.86	Dogar et al. (1999) ¹⁶
Western Rajasthan, India	Non-Pregnant females* Pregnant Mothers* Newborns				14 50 50	10.1 \pm 2.6 8.1 \pm 2.2 13.5 \pm 2.8	Kothari et al. (1991) ¹⁷

*They were matched for age, smoking habit, diet and body weight.

deficiency of vitamin C among Indian males compared to 13% among Indian females. This trend has been consistently observed in populations from USA, UK and Nigeria (Table-II). Underlying cause for this difference has not been established so far. However, smoking and use of drugs of abuse (more common among males) could be the possible reasons^{11,14} (*vide infra*). Moreover, males are also known to take less vitamin supplements.¹⁹

Effect of smoking on vitamin C: Tobacco smoking, both active and passive, could be a factor causing decreased ascorbic acid levels among human subjects. In a study conducted by Hampl et al., more smoking females than non-smoking females (25% to 7%, respectively) had plasma vitamin C levels less than 11 $\mu\text{mol/l}$.¹⁹ According to the same study, 31% male-smokers compared with 11% male non-smokers had vitamin C deficiency. As tobacco smoke contains a high oxidant content, it explains the low antioxidant status and increased oxidative stress that is consistently observed in smokers.^{25,26} In general, smokers compared to non-smokers eat more fat and less fiber, fruits and vegetables - a fact that could contribute to the depletion of ascorbic acid in smokers.²⁷⁻³²

Effect of drugs of abuse on vitamin C: Drug addiction among males may have a negative

influence on the plasma ascorbic acid levels. Ene-Obong et al. considered alcoholism among males to be one of the reasons for low serum ascorbic acid levels.²⁴ Marquez et al. assessed the relationship between consumption of drugs of abuse and plasma vitamin C levels and reported, that, out of 56 male chronic users of drugs of abuse with an age range of 16-40 years, 23.2% were at moderate risk (3.5 \pm 0.1 $\mu\text{g/ml}$) of vitamin C deficiency.³³ Likewise, classifying them on the basis of antioxidant status it was found that 55.4% had suboptimal or inadequate concentrations to carry out antioxidant protective function.³³

Prevalence of vitamin C deficiency among South Asians and contributing factors: It was observed that the mean plasma vitamin C levels of Indians / South Asians living abroad did not vary much compared with other ethnic groups (Tables-I and II), but there was a significant decrease in the plasma levels of vitamin C of Indians and Pakistanis living in India and Pakistan. The possible reason could be inadequate consumption of fruits and vegetables rich in vitamin C, especially by those belonging to the low socioeconomic group.²¹⁻²³ Contributory factors were large household size, low educational status, environmental pollution and absence of vitamin supplements.³⁴

Table-II: Comparison of serum ascorbic acid levels of males and females with different ethnic backgrounds in USA, UK and Nigeria

Place	Study Population	Age Range (Years)	Serum Ascorbic Acid Levels ($\mu\text{g/ml}$)				Study Group & Reference
			Males		Females		
			n	Mean \pm SD (Range)	n	Mean \pm SD (Range)	
Arizona, USA	Whites & Hispanics	6-92	144	5.40 \pm 2.5 (0.55-16.6)	350	5.8 \pm 2.3 (0.77-14.1)	Johnston et al. (1998) ¹⁸
USA	Non-Hispanic Whites, Non-Hispanic Blacks* and Mexican Americans	12-74	7355	(6.4-8.1)	8414	(7.4-9.7)	Hampl et al. (2004) ¹⁹
USA	College Students	23.1 \pm 6.5	61	7.6 \pm 3.0	73	8.1 \pm 2.6	Johston et al. (1998) ²⁰
USA	US Nationals	30-75	3347	8.69 (Median)	3724	11.3 (Median)	Loria et al. (2000) ²¹
Norwich, UK	UK Nationals	68-90	60	6.62 \pm 3.7 (0.779-14.6)	85	8.24 \pm 4.15 (1.11-16.3)	Bailey et al. (1997) ²²
Norwich,	US Nationals	65-95	785-	Free-Living	231-	Institution	Bates et al.
Enugu State Nigeria	School Children	10-20	30	7.1 \pm 2.1	60	8.6 \pm 2.9	Ene Obong et al. (2003) ²⁴

*Non-Hispanic black males had slightly increased risk of vitamin C deficiency compared to non-Hispanic White males.

**Greater burden of disease and age-related physiological abnormality may have compromised vitamin C status in these subjects.

The prevalence of vitamin C deficiency was noted to be highest among Indians and people of South Asian origin as compared to other races except a Mexican population³⁵ (Table-III). The following factors could be contributing to this observation:

- I. *Culinary styles and vitamin C*: Vitamin C is heat-labile, so differences in plasma levels may reflect differences in culinary styles.¹⁵ Methods of food preparation by South Asians substantially reduce the vitamin C levels. Cooking of vegetables and fruits can reduce their vitamin C content by 20 – 40%¹⁹, and at the same time, drying green leafy vegetables can eliminate the majority of water-soluble vitamins.³⁴
- II. *Lipoprotein metabolism and vitamin C*: Lower levels of vitamin C in South Asians may reflect an increased blood utilization of vitamin C due to decreased levels of HDL cholesterol, and increased need for antioxidant

activity probably because of genetic factors as well as their diet and eating habits.^{36,37} Moreover, an association between plasma level of ascorbic acid and HDL cholesterol has been reported³⁸. Since Pakistani population too, has a high prevalence (45.8%) of low-HDL cholesterol (serum levels <35mg/ml),³⁷ an increased need for antioxidant activity might be reflected by lower levels of vitamin C in this population.

- III. *Effect of H. pylori infection on vitamin C*: Helicobacter pylori is a gram negative, microaerophilic human pathogen which is prevalent worldwide. According to some community-based studies, more than half of adult population in developed countries and 90% of those in developing countries are infected with this bacterium.^{39,40} Among the Indians living in Singapore, its prevalence has been reported to be 53.2%.⁴¹

Unfortunately, no community-based studies have been carried out in Pakistan. However hospital-based data of dyspeptic patients indicate that prevalence of *H. pylori* in Pakistan is about 80%.⁴² Annibale et al. have recently reported that plasma level of vitamin C is lower in *H. pylori* infected group as compared to healthy controls.⁴³ Therefore, *H. pylori* infection could be another factor causing ascorbic acid deficiency among South Asians.

IV. Parasitic infections and vitamin C: Improperly washed vegetables may carry parasitic organisms and their eggs. These may be eaten with vegetables and fruits, making vegetarians susceptible to various parasites. In a study conducted by Mohamed and Beynen on camels, reduced levels of vitamin C were found in camels with parasite infections, especially in those with trypanosomiasis.⁴⁴ It is suggested that the low vitamin C status in infected camels is caused by increased utilization and/or decreased synthesis of vitamin C. This observation could hold true for human beings as well. Since parasitic infections are very common among South Asians,^{45,46} especially among Pakistanis,⁴⁷ it could be an important cause for vitamin C deficiency in these populations.

Seasonal variation in ascorbic acid levels: In a study conducted by Ness et al., plasma levels of vitamin C in men and women were found to be higher in winter (6.54±0.3 and 8.48±0.3µg/ml) than in summer (6.16±0.3 and 8.43±0.3µg/ml), respectively.¹⁵ Furthermore, Chiplonkar et al. observed a strong association between consumption of non-sweet fruits and plasma ascorbic acid levels.¹¹ As the availability of non-sweet fruits, namely oranges, grapefruits, guava, lime and strawberries is more in winter, it could explain the seasonal variation in the plasma vitamin C levels.¹¹

Genetics and vitamin C: Ness et al. consider that genetics plays a role in differences across racial groups,¹⁵ however, this hypothesis has been questioned by Hampl et al., who are of the opinion that dietary differences among

different ethnic groups are the major determinants of low ascorbic acid levels.¹⁹

The major genetic factor appears to be haptoglobin (Hp) – a hemoglobin-binding antioxidant that reduces the iron-mediated generation of free-radicals. A positive relationship between serum haptoglobin level and serum vitamin C concentration has been observed. This indicates that stability of L-ascorbic acid in plasma is directly proportional to haptoglobin concentration.^{48,49} Haptoglobin shows a genetic polymorphism with 3 phenotypes: Hp1-1, Hp 2-1, and Hp2-2. Reference serum haptoglobin concentrations are lower in Hp 2-2 subjects.⁴⁸ Both, the vitamin C and haptoglobin concentrations, have been found to be lowest in the serum from Hp 2-2 individuals. According to Langlois et al., 84.2% Indians, 51.3% Iranians and 54.8% of Thais carry Hp2-2 phenotype.⁴⁸ These results indicate that subjects who are Hp 2-2 type and consume a vitamin C-poor diet are most likely to develop vitamin C deficiency.

Compared to females, haptoglobin concentrations are lower among males, therefore, the stability of ascorbic acid is relatively low in the plasma of males. This may explain why males have low levels of plasma ascorbic acid compared to females and why they are more prone to developing vitamin C deficiency.

Vitamin C deficiency in Pakistan: To the best of our knowledge, there has been only one study carried out in Pakistan pertaining to ascorbic acid deficiency in Pakistani subjects with essential hypertension.¹⁶ The serum ascorbic acid levels of hypertensive males in the study were in the range of 0.86–5.22µg/ml, while the normotensive males in the same study had ascorbic acid levels in the range 3.52 – 7.12µg/ml. These values were comparable to the levels among Indians.¹¹ This could be because of similar lifestyles and economic status of the populations of the two countries. The significantly low serum ascorbic acid level in hypertensives suggests a positive correlation between high blood pressure and low plasma vitamin C level. It has been postulated that vitamin C increases prostacyclins (a potent vasodi-

Table-III: Prevalence of vitamin C deficiency (percentage of populations having plasma vitamin C levels less than or equal to 2 µg/ml) among different races or ethnic groups.

<i>Race/ Ethnicity (place)</i>	<i>% Vitamin C Deficient Population (Plasma ascorbic acid levels ≤ 2 µg/ml)</i>	<i>Study Group & Reference</i>
USA-Whites	6.5	Johnston et al. (1998) ¹⁸
- Hispanics	5.5	
- Others	5.1	
UK- Whites	5.5	Ness et al. (1999) ¹⁵
- African origin	3.7	
- South Asian origin	7.9	
USA - Non-Hispanics Whites	11.7	Hampl et al. (2004) ¹⁹
- Non-Hispanics Blacks	13.0	
- Mexican Americans	9.0	
Indian Males (Pune)	20.0	Chiplonkar et al. (2002) ¹¹
Indian Females (Pune)	13.0	
Indian Children (Bhopal)	2.6	Dwivedi et al. (1992) ¹²
Indian Malnourished Children (Jaipur)	1.1	Chainani et al. (1994) ¹³
Indian Males (Singapore)	17.8	Hughes et al. (1998) ¹⁴
Indian Females (Singapore)	11.0	
Malay Males (Singapore)	19.7	
Malay Females (Singapore)	7.7	
Chinese Males (Singapore)	14.4	
Chinese Females (Singapore)	0.7	
Mexican Females	39.0	Villalpando et al. (2003) ³⁵
Mexican Children	23.0	

lator); influences Na⁺/K⁺ ATPase pump, thereby stabilizing and protecting the biomembrane from peroxidative damage and at the same time affects cytosolic Ca⁺⁺ levels that regulate smooth muscle contractility of the peripheral blood vessels. These diverse actions of vitamin C explain the rise in blood pressure in vitamin C deficiency. It has also been suggested that smoking and high blood pressure could be associated with low ascorbic acid levels in South Asian men.¹⁵

A preliminary study recently carried out in our laboratory revealed that 65% of normal healthy Pakistani adults working at the Aga Khan University had plasma levels of ascorbic acid below 10 µg/ml (lower limit of normal plasma concentration of ascorbic acid) indicating that ascorbic acid status is low even among

the Pakistanis belonging to the middle class socio-economic structure of the society.⁵⁰ This problem, perhaps, would be more acute in people belonging to the lower socio-economic strata.

Guidelines from Food and Nutrition Board of National Academy of Sciences: According to the revised guidelines by the Food and Nutrition Board of National Academy of Sciences, the recommended dietary allowance (RDA) for vitamin C has been proposed to be 120 mg/day.⁵¹ Smokers, cancer patients and those with higher risk of developing coronary artery disease would, perhaps, require additional dietary and supplemental ascorbate.⁵²⁻⁵⁴ Vitamin C intake, whenever possible should come from fruits and vegetables and people should be encouraged to eat 5 servings of vegetables and

fruits daily.⁵¹ For those unable to or unwilling to consume fruits, vegetables, or vitamin C-fortified foods or beverages, a supplement containing 200 mg of vitamin C should be adequate.⁵¹

CONCLUSIONS

Simon et al. have shown a strong relationship between low serum ascorbic acid and mortality among US adults and have recommended that increasing the consumption of ascorbic acid could decrease the risk of death among Americans with low ascorbic acid intakes.⁵⁵ According to the IPCS INTOX data bank (www.intox.org), normal plasma concentrations of ascorbic acid are between 10-20 µg/ml. However, a vast majority of Pakistani normal healthy subjects in our preliminary study have values below this range alluding to the possibility that a large number of our normal healthy adults could be having plasma levels of ascorbic acid below the lower limit of the normal range for most Western populations.⁵⁰ Similar low values have also been reported by Hughes et al. in Chinese, Malays and Indians residing in Singapore.¹⁴ High proportion of individuals with low levels of ascorbic acid in Pakistani, Chinese, Malays and Indian populations compared to most Western populations (Table-III) might explain higher rates of cardiovascular disease in South Asians. In fact, an epidemic of cardiovascular disease has been reported in South Asians⁵⁶, and cancer is also regarded as a major noncommunicable disease in this region.⁵⁷

Lower intake of fresh fruits and vegetables and over-cooking (which destroys many water soluble vitamins, especially vitamin C) of our food could be contributing to high prevalence of cardiovascular disease and cancer in our population. A community based study involving a large sample size would be required to find out the prevalence of the deficiency of ascorbic acid in our population and to investigate whether or not there is any association of low levels of plasma ascorbic acid with cardiovascular disease and cancer in this population.

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