Original Paper

Vitamin C Status of an Outpatient Population

Carol S. Johnston, PhD, FACN and Lori L. Thompson, MS

Department of Family Resources and Human Development, Arizona State University, Tempe

Key words: ascorbic acid, vitamin C, depletion, deficiency, status

Objective: To determined the prevalence of vitamin C deficiency (plasma vitamin C concentrations less than 11.4 μmol/L) and vitamin C depletion (plasma vitamin C concentrations from 11.4 to less than 28.4 μmol/L) in an outpatient population.

Subjects and Methods: A consecutive sample of patients presenting at a health maintenance organization laboratory for outpatient procedures was utilized. Plasma vitamin C concentrations were determined in 350 females and 144 males, aged 6 to 92 years (mean ± SD: 46.7 ± 18.7 years).

Results: The mean plasma vitamin C concentration for all subjects was 32.4 ± 13.6 μmol/L. Mean plasma vitamin C did not vary by sex, race, or fasted state. Diabetics had a significantly lower mean plasma vitamin C concentration (25.6 ± 10.8 μmol/L) compared to patients presenting for general check-up/gynecological exams (33.5 ± 14.8 μmol/L) or pregnancy exams (32.4 ± 9.7 μmol/L). Six percent of subjects had plasma vitamin C concentrations indicative of vitamin C deficiency (n=31), and 30.4% of the sample were vitamin C depleted (n=150). The prevalence of vitamin C deficiency or vitamin C depletion did not differ by race or visit category.

Conclusions: Surprisingly high rates of vitamin C deficiency and vitamin C depletion were evident among generally healthy, middle class patients visiting a health care facility for routine health exams, gynecological exams, and pregnancy exams.

A large number of men in our army were attacked also by a certain pestilence, against which the doctors could not find any remedy in their art. A sudden pain seized their feet and legs; immediately afterwards the gums and teeth were attacked by a sort of gangrene, and the patient could not eat any more. Then the bones of the legs become horribly black, and so, after having continued pain, during which they showed the greatest patience, a large number of Christians went to rest on the bosom of our Lord.

—Jacques de Vitry, the First Crusade [1]

INTRODUCTION

Modern societies with year-round access to fresh fruits and vegetables, most of which are rich sources of vitamin C, seldom develop scurvy, and the disease is usually considered in a historical context. However, examination of the recent medical literature suggests that scurvy continues to be observed in developed nations. In adults, overt scurvy is preceded by lassitude, weakness, irritability, weight loss, and vague myalgias. Patients usually seek medical advice following the appearance of a skin rash and swelling of lower extremities. Cases may be initially misdiagnosed, usually as cutaneous vasculitis [2–5]. In patients, a negative skin biopsy, and a detailed inquiry about eating habits to disclose the absence of fresh fruits and vegetables, indicated scurvy [3–11]. The number of these recent case reports is surprising, and little research has been conducted to determine the prevalence of vitamin C deficiency in the US population.

Data compiled from the NHANES II survey (n=9873 nonsupplement users) demonstrated that although mean serum vitamin C levels were well within normal ranges for children, teenagers and adults, low serum vitamin C concentrations were observed in 25% of nonsmoking adult males 60 to 74 years of age [12]. Data from our laboratory indicated that the prevalence of vitamin C deficiency (plasma vitamin C<11.4 μmol/L [13,14]) was 2% in an apparently healthy, nonsmoking campus population (n=135; aged 24.4 ± 0.7 years; 73 females and 62 males) [15]. Vitamin C depletion (plasma vitamin C ranging from 11.4 to less than 28.4 μmol/L reflecting a moderate risk of developing vitamin C deficiency due to depleted body pool [13,14]) was noted in 16% of this campus population [15].

Address reprint requests to: Carol Johnston, PhD, FACN, Arizona State University, Box 872502, Tempe, AZ 85287-2502.

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These data prompted us to examine the vitamin C status of a local outpatient population.

METHODS

Study Population

Blood was collected from a consecutive sample of patients presenting at a local health maintenance organization laboratory, Cigna HealthCare of Arizona, for outpatient procedures (46.7 ± 18.7 years of age; range, 6 to 92 years; 144 males and 350 females). A majority of subjects were white (81%, n=398), and 11% of subjects (n=55) were Hispanic. For 10 consecutive working days, blood samples were taken from all patients with blood draws scheduled from 0800 to 1200 hours at a single laboratory. The diagnosis code was taken from laboratory forms. Routine health exams and gynecological exams accounted for 25% of these visits, and pregnancy exams accounted for 19% of visits. Six percent of subjects were diabetic, 4% of subjects had hyperlipidemia or coronary heart disease, and 8% of subjects presented with hypertension, rheumatoid arthritis, hypothyroidism or senile cataract. Approximately 29% of the subjects were fasting at the time of blood collection. The study was approved by the University Human Subjects Institutional Review Board at Arizona State University.

Vitamin C Analysis

Venous blood was collected in sodium EDTA-anticoagulated vacutainer tubes. Whole blood samples remained sealed and were held at room temperature for up to 5 hours prior to centrifugation. Ascorbic acid plus dehydroascorbic acid (collectively termed vitamin C) is stable in whole blood in unopened vacutainer tubes for up to 8 hours at room temperature [16]. Plasma was immediately acidified with 10% TCA (1:1 v/v) and stored at −45°C. Plasma vitamin C was determined within one week of blood collection using the 2,4-dinitrophenylhydrazine method of Omaye et al [17].

Statistical Analysis

Data are reported as the mean ± SD. Statistical analysis was by Kruskal-Wallis oneway analysis of variance for comparisons between patient groups in which distributions were nonparametric. The t-test for independent samples was used for comparisons by sex and fasting state. The chi-square test was used to examine the relationship between vitamin C status and race or visit category. P values <0.05 were considered significant. All analyses were performed using the Statistical Package for Social Sciences (SPSS/PC+, SPSS, Chicago, IL).

RESULTS

The mean plasma vitamin C concentration for all subjects was 32.4 ± 13.6 μmol/L (0.57 ± 0.24 mg/dL). Plasma vitamin C concentrations range from about 20 to 45 μmol/L when dietary intakes of vitamin C correspond to the recommended dietary allowance (RDA), 60 mg/day [14,18–20]; this wide range of concentrations reflects the sigmoidal nature of the plasma concentration versus dosage curve for vitamin C at this level of ingestion [18]. Mean plasma vitamin C concentrations were not different among females and males, 32.9 ± 13.1 and 30.7 ± 14.2 μmol/L, respectively. Plasma vitamin C concentrations ranged from 4.4 to 80.1 μmol/L in females and from 3.1 to 94.3 μmol/L in males (Figs. 1 and 2).

Consistent with the observation of others [12], mean plasma vitamin C concentrations were similar in fasting (n=142) and nonfasting (n=352) subjects. Mean plasma vitamin C did not differ by race (Table 1). However, mean plasma vitamin C was significantly lower in diabetics (n=31; 28 classified as Type II diabetics) vs. patients presenting for general check-up/gynecological exams or pregnancy exams (Table 2). This difference was not unexpected as others [21,22] have postulated that vitamin C status is compromised in diabetes.

Overall, 6.3% of the subjects had plasma vitamin C concentrations indicative of vitamin C deficiency (n=31, 95% CI: 6.8–8.5 μmol/L), and 30.4% of the sample were vitamin C depleted (n=150, 95% CI: 20.4–21.6 μmol/L). The prevalence of vitamin C deficiency did not differ by race, 6.5% and 5.5% for whites and Hispanics, respectively (Table 1). The prevalence of vitamin C deficiency was also similar across visit categories, ranging from 5.3% for pregnant women to 10.0% for hyperlipidemia/heart disease (Table 2). The prevalence of vitamin C depletion did not differ by race or visit category (Tables 1 and 2).

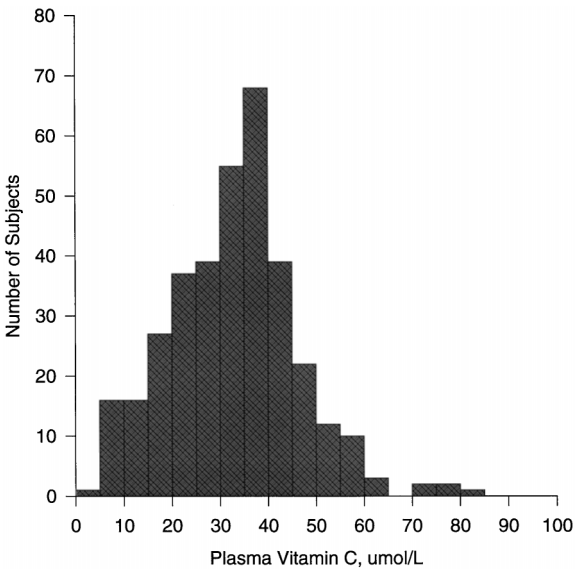

Fig. 1. Distribution of plasma vitamin C concentrations in females (n=350).

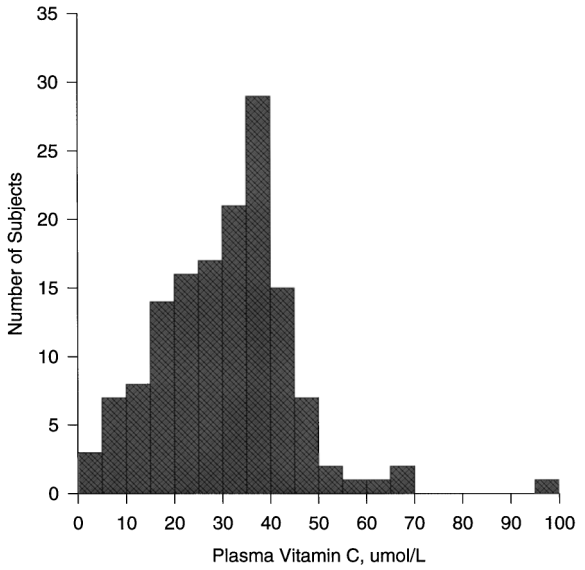

Fig. 2. Distribution of plasma vitamin C concentrations in males (n=144).

DISCUSSION

This study showed that vitamin C deficiency was present at surprisingly high rates among generally healthy patients visiting a health care facility for routine health exams, gynecological exams, and pregnancy exams. The poor vitamin C status of subjects may be a result of inadequate consumption of fruits and vegetables. Although dietary data was not available for subjects in the present study, we have demonstrated previously that vitamin C status was related to fruit and vegetable consumption and that vitamin C depleted subjects consumed significantly less servings of fruits and vegetables per day compared to subjects with adequate vitamin C status, 1.3 and 2.5 servings, respectively [23]. The second National Health and Nutrition Examination Survey reported that about 20% of Americans consumed less than 75% of the RDA for vitamin C daily [24].

Vitamin C status did not differ by race in the present study. The majority of our subjects were white and Hispanic, and recent data from a national survey indicated that median daily vitamin C intakes were similar for whites and Hispanics (75 mg); whereas, in comparison, non-Hispanic blacks consumed 10% less vitamin C daily (66 mg) [25].

The proportion of smokers in this outpatient population was not known. The poor vitamin C status of some of our subjects may be related in part to smoking. Schectman et al [26] reported that the prevalence of low serum vitamin C concentrations in smokers (n=4100) was 33.4% compared to 11.4% in nonsmokers (n=7482). A separate study of nonsupplement users noted that 50% of male smokers over 60 years of age and 25% of adult men and women smokers had low serum vitamin C concentrations [12]. It is clear that the vitamin C status of smokers needs to be improved. Individuals who smoke required over 200 mg vitamin C daily to maintain serum vitamin C concentrations at a level equivalent to nonsmokers consuming the RDA for vitamin C [26].

Several studies have reported vitamin C concentrations in critically ill patients. Hunt et al [27] reported that upon admission the mean plasma vitamin C concentration for elderly hospitalized patients with acute bronchitis (n=57) was 23.3 ± 22.7 μmol/L and that 35% of subjects had plasma vitamin C concentrations <11.4 μmol/L. In another study, median plasma vitamin C in patients in intensive care with life-threatening conditions ranging from accidental injury and surgery to major organ failure, 10.8 μmol/L, was significantly lower than that for hospital patients with less severe conditions such as diabetes, 44.9 μmol/L, and gastritis, 47.1 μmol/L [28]. Patients with definite or possible acute myocardial infarction and unstable angina (n=506) also had poor vitamin C status upon admission, 7.4 ± 1.7 μmol/L [29]. These studies indicate that the vitamin C status of critically ill patients is often compromised, a reflection most likely of increased vitamin C utilization and metabolism.

Vitamin C deficiency was noted in 6.3% of the outpatient sample, and plasma vitamin C ranged from 3.1 to 11.2 μmol/L in these subjects. Since less than 10 mg of vitamin C daily alleviates most symptoms of scurvy, advanced scurvy is only rarely observed in the US. The symptoms of early scurvy are vague and nonspecific but physiologically relevant. Shelton and Ryan [11] describe a case report of a young, seemingly healthy 20-year old woman diagnosed with scurvy (plasma vitamin C concentration, 5.7 μmol/L). The only physical signs of scurvy in this patient were several petechiae, an ecchymotic

Table 1. Plasma Vitamin C, Prevalence of Vitamin C Deficiency, and Prevalence of Vitamin C Depletion in an Outpatient Population Categorized by Ethnicity

Ethnicity		Plasma vitamin C	Prevalence of vitamin C deficiency (plasma vitamin C <11.4 μmol/L)		Prevalence of vitamin C depletion (plasma vitamin C 11.4 to <28.4 μmol/L)	
			%	mean ± SD (range)	%	mean ± SD (range)
	n	μmol/L		μmol/L		μmol/L
White	398	32.4±14.2*	6.5	7.8±2.3 (3.1–11.2)	30.4	20.9±4.8 (11.4–28.4)
Hispanic	55	31.8±12.5	5.5	6.5±1.6 (5.1–8.1)	34.5	21.1±4.3 (13.0–27.6)
Other	39	32.4±9.7	5.1	7.5±1.0 (6.8–8.2)	25.6	22.4±4.1 (16.3–28.2)

* Mean ± SD.

Table 2. Plasma Vitamin C, Prevalence of Vitamin C Deficiency, and Prevalence of Vitamin C Depletion in an Outpatient Population Categorized by Visit

Reason for visit		Plasma vitamin C,	Prevalence of vitamin C deficiency (plasma vitamin C <11.4 μmol/L)		Prevalence of vitamin C depletion (plasma vitamin C 11.4 to <28.4 μmol/L)	
			%	mean ± SD (range)	%	mean ± SD (range)
	n	μmol/L		μmol/L		μmol/L
General check-up, gynecological exam	124	33.5±14.8[a]*‡	6.5	7.3±1.9 (4.3–9.7)	27.4	20.5±4.7 (11.6–28.0)
Pregnancy exam	95	32.4±9.7[a]	5.3	8.1±2.4 (5.1–11.2)	26.3	23.8±3.6 (16.3–28.4)
Diabetes	31	25.6±10.8[b]	6.5	3.8±0.9 (3.1–4.4)	51.6	20.1±4.2 (11.9–26.1)
Hyperlipidemia; coronary artery disease	20	28.4±10.8[ab]	10.0	7.6±2.2 (6.0–9.2)	40.0	23.2±4.7 (16.5–28.4)
Other	224	32.9±14.2[a]	6.3	8.3±2.1 (4.4–11.1)	29.9	20.2±4.9 (11.4–28.4)

* Mean ± SD.

† Means with different superscripts differ significantly, $p<0.05$.

patch, and several corkscrew hairs located on the thighs. In a separate report, a young 12-year old girl with scurvy (plasma vitamin C concentration, 3 μmol/L) complained only of pain in the lower limbs and swelling of the gums [6]. Patients often report generalized weakness and fatigue in the months prior to hospital admission [2,8,9], symptoms commonly noted in the early phase of experimental scurvy [18,30].

CONCLUSIONS

In summary, the present study demonstrated that vitamin C depletion and vitamin C deficiency were evident in an outpatient population (prevalence rates, 30.4% and 6.3%, respectively). Symptoms associated with vitamin C deficiency are subtle but physiologically relevant. Efforts should be made to further establish the prevalence of poor vitamin C status in the US population and to delineate the clinical significance of below normal plasma vitamin C concentrations.

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