Review

Vitamin E status in healthy population in Asia: A review of current literature

Editor's Choice

Anku Malik[1], Manfred Eggersdorfer[2], and Geeta Trilok-Kumar[1]

[1] Institute of Home Economics, University of Delhi, India
[2] DSM Nutritional Products Ltd, Kaiseraugst, Switzerland

Abstract: Vitamin E is a lipid soluble antioxidant which mainly circulates as α-tocopherol in the human plasma. Its deficiency is associated with ataxia, neuropathy, anaemia and several other health conditions. Although substantial data on vitamin E status has been published worldwide, there is paucity of data on the extent of deficiency from most Asian countries, including India. Part of the problem is lack of validated biomarkers for vitamin E and no consensus on cut offs for defining deficiency and sufficiency. Thus, interpretation of the data on the vitamin E status is difficult. Limited available data from 31 studies on vitamin E status in healthy people from Asia, the most populated continent, has been collated for the purpose of this review. Broadly, the results suggest inadequate vitamin E status in most age groups, with the prevalence of deficiency reaching 67%, 80%, 56% and 72% in infants, children and adolescents, adults, elderly and pregnant women, respectively, based on varying cut offs. The findings are not surprising as both, vitamin E intakes and its status have not received too much attention in the past. Lack of conclusive data accentuates the need for more research on the vitamin E status across all age groups and to define age, gender and physiological state specific cut offs for vitamin E levels.

Keywords: vitamin E prevalence, healthy, vitamin E deficiency, tocopherol status, vitamin E status, Asia

Introduction

Vitamin E is a fat soluble biological antioxidant in the body that plays a key role in preventing conditions in which free radical mediated oxidative stress is implicated [1]. Other than its antioxidant activity, vitamin E also prevents hemolytic anaemia and neurological symptoms of vitamin E deficiency (ataxia, peripheral neuropathy [2], myopathy [3], pigmented retinopathy [4, 5]) and is associated with immune function and immunomodulation [6] as well as control of inflammation and regulation of gene expression [2]. Vitamin E has been used for its therapeutic role in for prevention of cancer [7, 8], improvement of cognitive performance [9], Nonalcoholic Fatty Liver Disease (NAFLD) [10] and Alzheimer's Disease [11], all of which need further substantiation with randomized controlled trials.

Vitamin E deficiency is not common in adults but seen more in children. The deficiency in children is mainly attributed to rapid growth coupled with limited stores in childhood allowing deficiency symptoms to become apparent [12]. The deficiency is not always an issue of poor dietary intakes; diseases leading to impaired fat malabsorption and conditions of oxidative stress such as malaria or HIV infections usually predispose humans to vitamin E deficiency [2]. Severe vitamin E deficiency occurs as a result of genetic abnormalities in the α-tocopherol transfer protein (α-TTP) resulting in ataxia with vitamin E deficiency [13]. α-TTP is a critical regulator of vitamin E status and it stimulates movement of vitamin E between membrane vesicles and facilitates secretion of tocopherol from hepatocytes [14]. Inadequate vitamin E intakes and deficiency have potential effects on health by increasing risk of cardiovascular disease and liver diseases [15–18].

While vitamin E comprises of eight naturally occurring forms (α-, β-, γ-, and δ-tocopherols and α-, β-, γ-, and δ-tocotrienols) and these tocopherols and trienols have been shown to contribute to vitamin E activity, the list is long and evidence of their role in vitamin E related functions is low. Thus, for the purpose of this review, we have included studies on α-tocopherol status of healthy individuals because alpha-tocopherol is the most biologically active form of vitamin E and accounts for 90% of the total tocopherols present in plasma based on the current diets in Asia [19].

Vitamin E sources and requirements

Though vitamin E occurs in various forms and in different proportions in foods, the main dietary sources of vitamin E

are edible vegetable oils. At least half of the tocopherol content of wheat germ oil, sunflower oil, cottonseed oil, safflower oil, canola oil, and olive oil is in the form of α-tocopherol. Other dietary sources providing vitamin E include unprocessed cereal grains, nuts, green leafy vegetables and meats, especially the fatty portion. [20].

The Dietary Reference Intakes (DRIs) for vitamin E were revised by the Food and Nutrition Board of the Institute of Medicine (2000) [20] on the basis of concentration of plasma α-tocopherol associated with normal in vitro hydrogen peroxide induced hemolysis. The data support an Estimated Average Requirement (EAR) of 12 mg (27.9 μmol) of α-tocopherol and Recommended Dietary Allowance (RDA) of 15 mg/day for all populations with a minimum age of 14 years with no increased allowances for pregnancy.

The adequate intake (AI) for infants (0–6 mo) was estimated to be 4 mg and for children aged 7–12 months, to be 5 mg [20]. In children, the EAR and RDA were extrapolated from the adult values accounting for lean body mass and growth requirement [20]. The RDA of 6 mg/day, 7 mg/day and 11 mg/day is applied for children in the age group of 1–3 years, 4–8 years and 9–13 years, respectively [20]. These recommendations are aimed at the prevention of symptomatic deficiency such as peripheral neuropathy [20] rather than health promotion or disease prevention.

Vitamin E status

The Food and Nutrition Board of Institute of Medicine [20] accepted circulating α-tocopherol concentration as the indicator of vitamin E status. Based on their recommendations, concentrations of circulating α-tocopherol that are < 12 μmol/L indicate vitamin E deficiency. There is currently no broadly accepted cut off point for optimal vitamin E status while a recent publication proposed that vitamin E levels of 30 μmol/L and above as optimal which was based on the health benefits like reduced risk for coronary heart disease [5]. However, no clear cutoffs for optimal levels of vitamin E have been defined.

There are also several limitations and challenges in interpretation of vitamin E status because of several reasons. Circulating α-tocopherol concentrations do not correlate well with the α-tocopherol intakes. Secondly, circulating α-tocopherol levels are highly influenced by a variety of factors including age, gender, dietary habits, smoking, drugs, obesity and pregnancy [2, 21, 22] and, finally, α-tocopherol concentrations are highly dependent on the type and amount of lipids in the diet as well as on the blood lipids including cholesterol, thereby making interpretation of the vitamin E status complex [19].

Vitamin E circulates in the blood mainly with LDL and is highly correlated with blood lipids, especially cholesterol. As soon as the concentration of serum lipids increases, vitamin E partitions out of the cellular membrane compartments and moves into the circulating lipoproteins. Thus, during pathological conditions where serum lipid concentrations are increased, vitamin E deficiency may be misinterpreted if the lipid concentrations are not taken into account [2]. For this reason, α-tocopherol:total cholesterol ratios have more recently been used to assess vitamin E status. By expressing vitamin E as a ratio of circulating lipid concentration, a more accurate assessment of vitamin E status is obtained [23]. In subjects with altered lipid levels due to liver disease or other health conditions, it is important to present both the absolute α-tocopherol and the α-tocopherol:lipid ratio for optimal assessment of status. In terms of ratio of α-tocopherol: total cholesterol, the cut off is < 2.2 μmol/mmol [24] and < 1.59 μmol/mmol for α-tocopherol:total cholesterol and triacylglecerol, indicating vitamin E deficiency [25].

Data from the third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) indicates that the α-tocopherol:total cholesterol ratio is a better indicator of vitamin E status in healthy individuals when compared to α-tocopherol alone [2]. However, the ratios should be interpreted with caution in children, especially those who are malnourished and have multiple micronutrient deficiencies. Since this review covers studies conducted on apparently healthy populations, we have included the concentrations of α-tocopherol alone as well as ratios.

Vitamin E status in Asia

Although a large proportion of countries in Asia are low to middle income with high prevalence of micronutrient deficiencies, the vitamin E status and prevalence of vitamin E deficiency is almost unknown because of paucity of studies conducted in this continent. A review published in 2011, found only 19 population-based assessments of vitamin E status from low- to middle-income countries of the world conducted between 1992 and 2009 (11, 3 and 5 studies among children, elderly and groups of mixed ages, respectively) [2]. Based on a plasma α-tocopherol concentration cutoff that varied from 12 to 14 mmol/L, the prevalence of vitamin E deficiency ranged from 6% to 70% in children, 27% to 55% among elderly and 4% to 70% in the mixed age group [2, 26]. Although substantial research has been published on vitamin E status worldwide, which was systematically reviewed recently [5], there is no national data describing the extent of vitamin E deficiency in India, or for that matter in the Asian subcontinent. The main constraint in determining the status of vitamin E and its role in human health is the lack of validated biomarkers for assessment of vitamin E status [27].

With limited data describing the extent of vitamin E deficiency in Asia, this review aims to collate the current data available on vitamin E status in healthy Asian population and to understand the extent of vitamin E deficiency across all age groups. Additionally, we want to highlight the need for research to assess vitamin E intake and status in healthy humans and its role in public health.

Methods

Criteria for identification and selection of studies

To identify relevant articles, two independent researchers searched Pubmed databases for selected peer reviewed articles in English from 2000 to 2018. Terms such as vitamin E prevalence, healthy, vitamin E deficiency, tocopherol status, Vitamin E status and Asia as well as combinations of these terms were entered in the database. Studies conducted on apparently healthy Asian populations reporting serum or plasma α-tocopherol levels were included. We excluded case control studies, randomized controlled trials, case reports, systematic reviews and meta-analysis. Baseline vitamin E levels in observational studies conducted on healthy populations were also included. Title, abstract and full text articles were identified and assessed for eligibility after applying the inclusion and exclusion criteria. Critical appraisal for each study eligible for inclusion was done by both researchers. After agreement on the content of the study, 31 studies out of total of 1641 studies were shortlisted. A flow chart of the selection process is presented in Figure 1.

The shortlisted studies were tabulated into different population groups, including infants, children and adolescents, pregnant women, adults and elderly population aged $\geq$ 60 years.

Vitamin E level was expressed in μmol/L in this review and any values expressed in μg/dl, mg/dl and mg/L were converted to μmol/L, using the conversion factor of 0.02322, 23.22 and 2.322, respectively.

Results

Vitamin E status of Asian children, adolescents, pregnant women, adults and elderly from various parts of Asia are listed in the following tables (Tables 1–4).

For the purpose of this review, both age groups and mean ages have been reported. Medians have been reported wherever available. High Performance Liquid Chromatography (HPLC) was the most common method used for assessment of α-tocopherol in the serum or plasma. We reported mean BMI wherever available, since obesity could predispose an individual to vitamin E deficiency due to sequestration of α-tocopherol in adipose tissue [2]. Most studies reported the vitamin E status as mean α-tocopherol level and mean ratio of α-tocopherol:total cholesterol while only a few used median with interquartile range; those reporting percentage of vitamin E deficient participants in the sample population (% deficiency) used various cut-offs for defining vitamin E deficiency. Because of the wide variation in the biomarkers and cutoffs used to define vitamin E deficiency, direct comparison of the prevalence of deficiency in the studied population is not possible. Nonetheless, these studies provide an indication of the extent of deficiency and suboptimal vitamin E status.

Vitamin E status in infants, children and adolescents

Majority of the available studies on the prevalence of vitamin E deficiency in Asia are on infants, children and adolescents. However, the studies that were included in this review had age ranges that were very large, without a clear rationale for selecting these age ranges. Therefore, vitamin E status in infants, children and adolescents could not be tabulated separately. In the absence of homogeneity in age ranges used, we reported all studies covering the three age groups under birth to $\leq$ 18 years (Table 1).

With a lot of disparity in the cut offs for deficiency of α-tocopherol (4.8 to 15.0 μmol/L) in plasma used by various authors, varying mean levels of α-tocopherol and wide age ranges (birth to 20 years), comparison between various studies are difficult.

Vitamin E levels in cord blood at birth were lower than those in the maternal blood on the first day post delivery [15.9 (11.08) vs 25.7 (10.38) μmol/L [28]] indicating low placental tocopherol transfer. Living in rural areas increased the prevalence of vitamin E deficiency among rural children as compared to urban [27.1% vs 20%]; when assessed in terms of α-tocopherol: lipid ratio, all the children were vitamin E deficient [29]. Lower mean α-tocopherol levels were observed in males than females [30, 31, 32]. Mean vitamin E ranged between 7.4 (4.6) μmol/L [29] to 25.40 (7.01) μmol/L [30] and the prevalence of vitamin E deficiency reached as high as 67% [33] in this group. With a wide variation in values that defined deficiency due to large age ranges used in various studies, no comparisons could be made on the proportion of newborns, infants and children that are deficient across studies and countries.

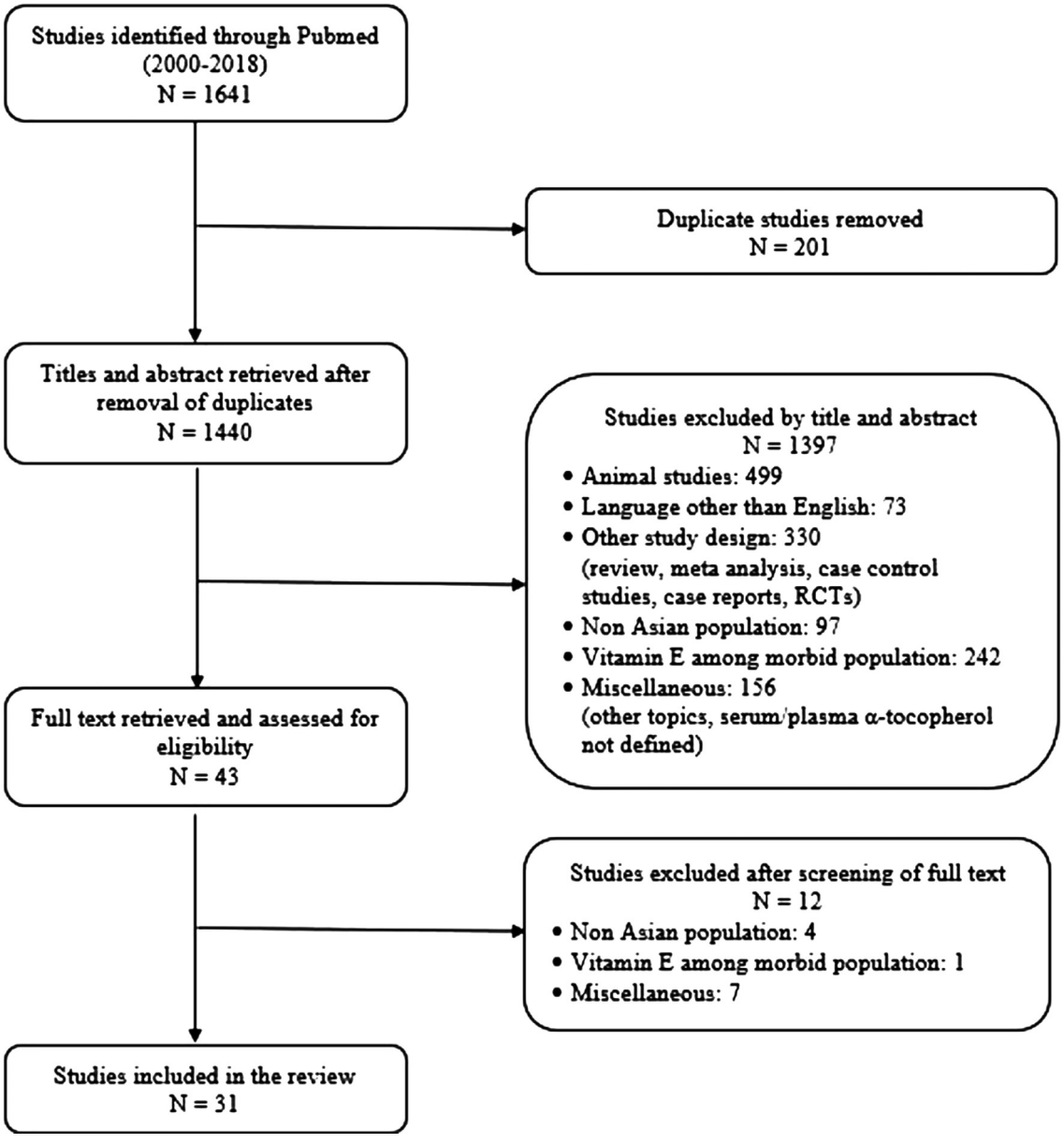

Figure 1. Flow chart of selection process.

Vitamin E status of pregnant women

Table 2 provides the data on vitamin E status of pregnant women in Asia. Only six studies fulfilled our inclusion criteria, five out of which were conducted on women in their first trimester.

Plasma α-tocopherol concentration of < 12.0 μmol/L is generally used to define vitamin E deficiency in normal, healthy adults [20]. There is no consensus on the definition of vitamin E deficiency in pregnant women because α-tocopherol concentration increases with blood lipids over the course of pregnancy. Using the cut off used for adult women of < 12.0 μmol/L, the proportion of women with deficient vitamin E levels varied from 58 % [34] to 72 % [35] with the mean tocopherol levels of 10.68 (8.01) μmol/L [34] and median value of 10.04 (8.07,12.35) μmol/L α-tocopherol [35]. However, when using 9.3 μmol/L as the cut off used by some authors for defining vitamin E deficiency, the proportion of women with vitamin E deficiency varied from 25 % [36] to 43.5 % [37]. Mean plasma vitamin E levels in this group ranged between 10.68 (8.01) μmol/L [34] to 66.45 (13.6) μmol/L [38].

Table 1. Vitamin E status in infants, children and adolescents.

Publication	Location	n (SEX)	Age (years) Range/Mean (SD)	Assay Method	Definition of Deficiency (i) α-Tocopherol (μmol/L) Or (ii) α-Tocopherol: total cholesterol (μmol/mmol)	% Deficiency	Mean (SD) plasma/serum α-Tocopherol (μmol/L)	Mean (SD) α-tocopherol: total cholesterol (μmol/mmol)	BMI (kg/m^2) Mean (SD)
Wang et al, 2009 [28]	China	143 (Mother Neonate pairs) Infants (M/F)	Maternal: 1 day postpartum 24.6 (3.76) Infant: At birth (cord blood)	HPLC	–	–	Maternal 25.7 (10.38) Cord plasma 15.9 (11.08)	–	–
Ulak et al, 2016 [55]	Bhaktapur, Nepal	467 (M/F)	2–12 mo[a] 6.8 (2.9)	Liquid Chromatography Tandem mass spectrometry	(i) Marginal < 18.9 Deficient < 9.3	36% 1.3%	20.6 (4.9)	–	–
Sirivichayakul et al, 2001 [30]	Bangkok, Thailand	66 (M: 37, F: 29)	196–257 days[a] 223.61 (9.97)	HPLC	(i) High < 40 Normal: 15–40 Deficient < 15	3.0% 92.4% 4.5%	T: 25.40 (7.01) M: 24.56 (6.73) F: 26.47 (7.35)	–	16.25 (1.43) M: 16.57 (1.56) F: 15.85 (1.16)
Giraud et al, 2008 [33]	Kwangju, Korea	131 (M: 65, F: 66)	2–6[a] 4.1 (1.3)	HPLC	(i) Deficient < 12.0	67%	2 yr: 11.9 (2.3) 3 yr: 10.5 (2.1) 4 yr: 10.4 (2.0) 5 yr: 10.9 (1.7) 6 yr: 10.2 (2.0)	–	–
Al-saleh et al, 2006 [31]	Al Kharj Saudi Arabia	513 (M: 258, F: 255)	3–16[a] 9.8 (3.3)	HPLC	(i) Deficient < 11.6[d]	3.1%	T: 20.20 (4.87)[d] M: 19.97 (5.34)[d] F: 20.67 (4.64)[d]	–	21.1 (25.1)
Kang et al, 2004 [32]	Taiwan	1773 (M: 862, F: 911)	4–18[a]	HPLC	(i) Deficient < 11.6	(ii) M: 2.37%	4–6 yrs: M: 15.1 (0.6) F: 16.5 (1.0)	4–6 yrs: M: 2.99 (0.05) F: 3.08 (0.18)	–
					(ii) Deficient < 1.59 (Tocopherol: cholestrol&TG)	F: 2.60%	7–12 yrs: M: 14.1 (0.4) F: 14.8 (0.4) 13–18 yrs: M: 13.4 (0.5) F: 14.4 (0.5)	7–12 yrs: M: 2.80 (0.08) F: 2.89 (0.04) 13–18 yrs: M: 2.83 (0.15) F: 2.83 (0.12)	

(Continued on next page)

Table 1. (Continued)

Publication	Location	n (SEX)	Age (years) Range/Mean (SD)	Assay Method	Definition of Deficiency (i) α-Tocopherol (μmol/L) Or (ii) α-Tocopherol: total cholesterol (μmol/mmol)	% Deficiency	Mean (SD) plasma/serum α-Tocopherol (μmol/L)	Mean (SD) α-tocopherol: total cholesterol (μmol/mmol)	BMI (kg/m^2) Mean (SD)
Schulze et al, 2014 [56]	Nepal	1000 (M/F)	6–8[a] 7.5 (0.4)	HPLC	(i) Marginal < 12.0 Deficient < 9.3	52.1% 17.9%	12.2 (3.3)	4.05 (0.85)	14.0 (1.0)
					(ii) Deficient < 2.2	0.6%			
West et al, 2015 [26]	Nepal	500 (M/F)	6–8[a]	r-P HPLC	(i) Deficient < 12.0 Moderately deficient < 9.3	54.8% 17.6%	12.1 (3.2)	–	–
Mai et al, 2003 [29]	South Vietnam	284 (F)	7–9[a]	HPLC	(i) Deficient < 4.8	R: 27.1% U: 20.0%	R: 7.4 (4.6) U: 9.0 (4.6)	R: 1.48 (0.91) U: 1.63 (0.83)	–
		Rural: 148 Urban: 136			(ii) Deficient < 2.36 (tocopherol: cholesterol & triacylglycerol)	R: 100% U: 100%			
Al-saleh et al, 2007 [21]	Al-Kharj, Saudi Arabia	349 (M/F)	10–20[a]	r-P HPLC	(i) Deficient: 12.54–26.70[d]	–	19.50 (4.41)[d]	–	–

M: Male, F: Female, T: Total, mo: months, yr: year, R: Rural, U: Urban, r-P HPLC: Reverse Phase High Pressure Liquid Chromatography, TB: Time of birth, TFF: Time of full feeding, TT: Term post menstrual age, TG: Triglycerides

[a]Age group;
[b]Median (interquartile range);
[c]original data in μg/dl , converted into μmol/L by multiplying 0.02322;
[d]original data in mg/dl, converted into μmol/L by multiplying 23.22;
[e]original data in μg/ml, converted into μmol/L by multiplying 2.322;
[f]original data in mg/L, converted into μmol/L by multiplying 2.322;
[g]Standard Deviation (SD) not given.

Table 2. Vitamin E status in pregnant women.

Publication	Location	n (Trimester)	Age (years) Range/Mean (SD)	Assay Method	Definition of Deficiency	% Deficiency	Mean (SD)	Mean (SD)	BMI (kg/m^2)
					(i) α-Tocopherol (μmol/L) Or (ii) α-Tocopherol: total cholesterol (μmol/mmol)		plasma/serum α-Tocopherol (μmol/L)	α-Tocopherol: total cholesterol (μmol/mmol)	Mean (SD)
Andert et al, 2006 [39]	Northeast Thailand	94 First trimester	15–41[a]	r-P HPLC	–	–	Primiparous 17.04 (4.29)	–	Primiparous 20.5 (2.6)
		Primiparous 51	Primiparous 23.1 (5.2)				Multiparous 17.13 (4.65)		Multiparous 23.9 (4.6)
		Multiparous 43	Multiparous 29.3 (4.9)						
Hammouda et al, 2013 [38]	Saudi Arabia	1106 First trimester	16–50[a] 27.9 (6.2)	r-P HPLC	–	–	Mothers of (N) infants 66.45 (13.6)[f]	–	Mothers of (N) infants 25.30 (5.2)
		Mothers of Normal (N) infants: 961					Mothers of (CM) infants 56.54 (16.93)[f]		Mothers of (CM) infants 28.85 (4.6)
		Mothers of Congenital malformation (CM) infants: 48							
Jiang et al, 2005 [36]	Nepal	1165 First trimester 10.9 (4.6) wks	23.6 (6.0)	r-P HPLC	(i) Deficient < 9.3	25%	12.12 (4.04)	–	19.3[g]
Shamim et al, 2013 [37]	Bangladesh	285 First trimester 10 weeks (8–12)[b]	>20 yrs	r-P HPLC	(i) Deficient < 12.0 < 9.3	70.2% 43.5%	10.04 (10.0, 10.8)[b]	–	–
Shamim et al, 2015 [35]	Bangladesh	1605 First trimester 10 weeks (8–12)[b]	<20 yrs: 770 20–29: 664 >30 yrs: 170	r-P HPLC	(i) Deficient < 12.0	72.3%	10.04 (8.07, 12.35)[b]	3.06 (2.53–3.56) [b]	BMI < 18.5 N = 707 (44.1%)
Asemi et al, 2010 [34]	Kashan, Iran	147 5–9 mo gestation	18–35[a]	r-P HPLC	(i) Deficient < 11.6[e] Normal > 11.6[e]	58.63% 41.37%	T: 10.68 (8.01)[e] (n = 145) Deficient: 4.99 (3.02)[e] Normal: 18.74 (5.34)[e]	–	–

M: Male, F: Female, T: Total, mo: months, yr: year, r-P HPLC: Reverse Phase High Pressure Liquid Chromatography
[a]age group;
[b]Median (interquartile range);
[c]original data in μg/dl , converted into μmol/L by multiplying 0.02322;
[d]original data in mg/dl, converted into μmol/L by multiplying 23.22;
[e]original data in μg/ml, converted into μmol/L by multiplying 2.322;
[f]original data in mg/L, converted into μmol/L by multiplying 2.322;
[g]Standard Deviation (SD) not given.

Vitamin E levels decreased as pregnancy progressed with authors reporting lower mean α-tocopherol values in the second or third trimester when compared to those in first trimester of pregnancy [10.68 (8.01) μmol/L [34] vs 66.45 (13.6) μmol/L, respectively [38]. No differences in mean tocopherol values between primiparous and multiparous women were observed [17.04 (4.29) μmol/L vs 17.13 (4.65) μmol/L, respectively] [39]. Healthy pregnant mothers giving birth to infants with congenital malformations had lower serum α-tocopherol when compared to healthy mothers of normal infants [56.54 (16.93) μmol/L vs 66.45 (13.6) μmol/L [38]] indicating effect of oxidative stress on congenital malformations.

Vitamin E status of adults

A total of 13 studies on healthy adults fit our inclusion criteria (Table 3) but again, wide age ranges used by some researchers made segregation of elderly and adults difficult, resulting in inclusion of data on elderly with adults under this section. The age ranges included in this section are from 16 to 75 years; ages have been reported either in means or ranges, with one study reporting median and interquartile ranges.

The overall mean α-tocopherol levels ranged between 15.14 (6.84) μmol/L [40] to 32.0 (1.0) μmol/L [41], with proportion of vitamin E deficient adults reaching 80% [42]. Mean α-tocopherol levels increased with increase in socio economic status, the highest levels reported in the highest income group [15.79 (11.61) μmol/L] [42]. Large proportion (80%) of adults from the low income population were deficient [42]. Vitamin E deficiency varied by sex and age across several studies with mean serum α-tocopherol values (μmol/L) higher in males as compared to females, respectively [18.1 (5.8) vs 15.6 (1.4) μmol/L [43]], [21.3 (0.6) vs 17.3 (0.5) μmol/L [44]]; and lower in younger adults [18.1 (0.7) μmol/L for $\leq$ 30 years vs 23.2 (0.9) μmol/L for > 30 years [44], [24.61 (0.0) μmol/L for < 35 years vs 25.08 (0.93) μmol/L between 46–55 years [45]].

When α-tocopherol was adjusted for plasma cholesterol concentration, the mean α-tocopherol:cholesterol ratio ranged between 3.13 (1.50) μmol/mmol [42] to 5.1 (0.1) μmol/mmol [44]. Higher α-tocopherol:cholesterol ratio was reported in men compared to women [3.13 (1.50) vs 3.06 (0.77) μmol/mmol [40]], [3.81 (0.85) vs 3.60 (0.22) μmol/mmol [43]], [5.6 (0.2) vs 4.3 (0.1) μmol/mmol [44]], [4.81 (10.74) vs 4.58 (9.87) μmol/mmol [46]] suggesting greater antioxidant protection for males against lipid peroxidation.

The proportions of adults deficient or sufficient in vitamin E were reported on the basis of different cutoffs for deficiency and thus no comparisons could be made.

Vitamin E status in elderly

Five studies matched our selection criteria (Table 4). Although individuals over 60 years are theoretically at higher risk of deficiency, considerable variability in definition of deficiency in published studies of the elderly makes it challenging to draw clear conclusions regarding the extent of vitamin E deficiency among this group.

Mean reported α-tocopherol levels in the elderly ranged from 22.10 μmol/L [47] to 27.12 (0.47) μmol/L [1]. Elderly women had a lower risk of inadequate vitamin E levels in terms of α-tocopherol and tocopherol:cholesterol ratio as compared to elderly men and mean α-tocopherol levels were higher in females as compared to males [26.01 (1.16) vs 22.99 (1.63) μmol/L [45]], [23.78 (0.74) vs 18.96 (0.74) μmol/L [47]], [26.4 (2.3) vs 20.0 (0.6) μmol/L [32]], [29.33 (0.67) vs 25.07 (0.35) μmol/L respectively [1]]. Similarly, α-tocopherol:cholesterol concentration was also reported to be higher in elderly women than in men [1, 32]. Considerable heterogeneity was found in the proportion of elderly with insufficient vitamin E status [2.91% [1] to 55.5% [48]], primarily due to different indicators and cut offs used to define deficiency.

Discussion

The term vitamin E collectively refers to eight structurally related isomers, of which α-tocopherol is the predominant form in blood that is exclusively obtained from diet. Bioavailability of vitamin E is influenced by several non-modifiable (gender, age and genetic constitution) and modifiable (lifestyle and intake of vitamin E) factors. Numerous other factors also affect its bioavailability including dietary factors, such as composition of the food matrix or the presence of fat and processes such as emulsification, incorporation into mixed bile salt micelles, transport through the unstirred water layer, uptake by the enterocyte, incorporation into intestinal lipoproteins, and secretion out of the intestinal cell into the lymph or into the portal vein. [49, 50, 51]. The deficiency of vitamin E is characterized by progressive peripheral neuropathy, ataxia, muscle weakness, retinal damage leading to vision loss, infertility and dementia [52, 53]. With several health implications associated with vitamin E deficiency, this review attempts to collate the existing data on vitamin E status in Asia.

It includes studies conducted in Asia to assess vitamin E status that reported either mean or median α-tocopherol or the proportion that were deficient based on mixed cut offs. Interpretation of the plasma α-tocopherol values is, however, challenging because plasma vitamin E concentration does not necessarily reflect intake or tissue reserve because

Table 3. Vitamin E status in adults.

Publication	Location	n (Sex)	Age (years) Range/mean (SD)	Assay Method	Definition of deficiency (i) α-Tocopherol (μmol/L) Or (ii) α-Tocopherol: total cholesterol (μmol/mmol)	% Deficiency	Mean (SD) plasma/serum α-Tocopherol (μmol/L)	Mean (SD) α-Tocopherol: total cholesterol (μmol/mmol)	BMI (kg/m^2) Mean (SD)
Al-saleh et al, 2007 [57]	Al Kharj, Saudi Arabia	743 (M/F)	16.1–71.3[a]	r-P HPLC	(i) Deficient < 11.6[d]	2.3%	T: 24.46 (7.5)[d] (n = 737) M: 24.75 (8.0)[d] F: 24.17 (7.06)[d]	–	27.42 (5.91)
Abiaka et al, 2008 [43]	Oman	250 (M: 130, F: 120)	M: 18–62[a] 30.3[g] F: 18–60[a] 32.3[g]	r-P HPLC	No cut off provided	(i) < 5% (ii) < 5%	T: 16.9 (4.4) M: 18.1 (5.8) F: 15.6 (1.4)	T: 3.71 (0.64) M: 3.81 (0.85) F: 3.60 (0.22)	–
Abiaka et al, 2002 [44]	Kuwait	260 (M: 159, F: 101)	18–63[a] 33.3[g] M: 18–58[a] 32.5[g] F: 18–63[a] 33.3[g]	r-P HPLC	(i) Deficient < 11.6	–	T: 20.0 (0.05) M: 21.3 (0.6) F: 17.3 (0.5) <30 yr: 18.1 (0.7) >30 yr: 23.2 (0.9)	T: 5.1 (0.1) M: 5.6(0.2) F: 4.3 (0.1) <30 yr: 4.7 (0.2) >30 yr: 5.8 (0.2)	–
Kang et al, 2004 [32]	Taiwan	1479 (M: 680, F: 799)	19–64[a]	HPLC	(i) Deficient < 11.6 (ii) Deficient < 1.59 (Tocopherol: cholesterol & TG)	(ii) 19–44 yrs: M: 0.93% F: 1.17% 45–64 yrs: M: 1.05% F: 1.31%	19–44 yrs: M: 18.0 (0.5) F: 18.8 (0.6) 45–64 yrs: M: 20.7 (1.3) F: 25.3 (1.4)	19–44 yrs: M: 2.93 (0.05) F: 3.38 (0.09) 45–64 yrs: M: 3.13 (0.16) F: 3.48 (0.09)	–
Al-saleh et al, 2007 [21]	Al-Kharj, Saudi Arabia	20–30 yrs: 219 >30 yrs: 426 (M/F)	20–30[a] >30[a]	r-P HPLC	(i) 20–30 yrs: 13.70–33.67[d] >30 yrs: 15.09–39.24[d]	–	20–30 yrs: 22.76 (7.20)[d] >30 yrs: 26.47 (7.66)[d]	–	–
Kim and Cho, 2015 [40]	Seoul, South Korea	106 (M: 33, F: 73)	20–59[a] 33.4 (10.6)	HPLC	(i) Deficient < 12.0 (ii) Deficient < 2.22	(i) 22.6% (ii) 9.0%	T: 15.14 (6.84) M: 15.45 (10.16) F: 15.00 (4.54)	T: 3.13 (1.50) M: 3.13 (1.50) F: 3.06 (0.77)	T: 22.7 (2.9) M: 23.1 (2.7) F: 22.5 (23.2)
Hiraoka, 2001 [41]	Japan	150 (F)	21–22[a]	HPLC	–	–	32.0 (10.5)	–	–
Boonsiri et al, 2007 [58]	Northeast Thailand	294 20–45 yr: 168 46–75 yr: 126	23–75[a] M: 46 (44.77, 47.03)[b] F: 44 (42.41, 44.64)[b] (M: 176, F: 118)	r-P HPLC	–	–	T: 26.64 (14.85) M: 28.60 (14.34) F: 23.72 (15.16) 20–45 years: T: 26.79 (14.84) M: 28.97 (13.92) F: 24.45 (15.51) 46–75 years: T: 26.44 (14.91) M: 28.24(14.81) F: 22.13 (14.44)	–	–

(Continued on next page)

Table 3. (Continued)

Publication	Location	n (SEX)	Age (years) Range/Mean (SD)	Assay Method	Definition of Deficiency (i) α-Tocopherol (μmol/L) Or (ii) α-Tocopherol: total cholesterol (μmol/mmol)	% Deficiency	Mean (SD) plasma/serum α-Tocopherol (μmol/L)	Mean (SD) α-tocopherol: total cholesterol (μmol/mmol)	BMI (kg/m^2) Mean (SD)
Zou et al, 2014 [59]	Japan	206 (M)	23–67[a]	r-P HPLC	–	–	T: 15.1 (3.9, 37.76)[bf]	–	T: 23.6 (16.1, 37.2)[b]
		< 40 yrs: 94					< 40 yrs: 15.1 (3.9, 31.81)[bf]		< 40 yrs: 23.5 (16.1, 35.8)[b]
		>40 yrs: 112					>40 yrs: 16.02 (3.9, 37.76)[bf]		>40 yrs: 23.6 (16.5, 37.2) [b]
Obeid et al, 2006 [46]	Beirut, Lebanon	857 (M: 319, F: 538)	25–64[a] 43.7 (11.1)	HPLC	(i) Deficient < 5.80[c]	0.7%	T: 24.54 (11.38)[c]	T: 4.67 (10.16)	T: 29.0 (5.80)
		M: 44.1 (11.5)			Low: 5.80–11.61[c]	3.7%	M: 24.72 (12.24)[c]	M: 4.81 (10.74)	M: 28.8 (4.90)
		F: 43.5 (10.9)			Accept: 11.61–37.2[c]	85.6%	F: 24.45 (10.86)[c]	F: 4.58 (9.87)	F: 29.1 (6.30)
					High > 37.2[c]	9.9%			
					(ii) Deficient < 2.5	4.1%			
Sripanidkulchai et al, 2003 [45]	Northeast Thailand	414 (M: 189, F: 325)	< 35 yrs: 41	HPLC	–	–	<35 yrs: T: 24.61 (0.0)[d]	–	–
							M: 25.54 (1.86)[d]		
							F: 23.92 (1.39)[d]		
			36–45 yrs: 223				36–45 yrs: T: 25.08 (0.70)[d]		
							M: 26.24 (1.16)[d]		
							F: 24.15 (0.70)[d]		
			46–55 yrs: 150				46–55 yrs: T: 25.08 (0.93)[d]		
							M: 23.92 (1.16)[d]		
							F: 26.24 (1.39)[d]		
Kieu et al, 2002 [42]	Vietnam	296 (M: 111, F: 185)	40–59[a]	HPLC	(i) Deficient < 4.64[c]	HIG: 55% M:55%	HIG: 15.79 (11.61)[c]	–	HIG: M: 22.5 (2.6)
						F: 54%			F: 22.4 (3.5)
		HIG – 98				MIG: 65% M: 63%	MIG: 12.54 (8.82)[c]		MIG: M: 21.2 (3.3)
						F: 66%			F: 21.4 (3.7)
		MIG – 98 LIG – 100			Marginal: 4.64–13.83[c]	LIG: 80% M: 90% F: 87%	LIG: 10.68 (7.0)[c]		LIG: M: 19.5 (2.3) F: 19.9 (2.9)

(Continued on next page)

Table 3. (Continued)

Publication	Location	n (SEX)	Age (years) Range/Mean (SD)	Assay Method	Definition of Deficiency (i) α-Tocopherol (μmol/L) Or (ii) α-Tocopherol: total cholesterol (μmol/mmol)	% Deficiency	Mean (SD) plasma/serum α-Tocopherol (μmol/L)	Mean (SD) α-tocopherol: total cholesterol (μmol/mmol)	BMI (kg/m^2) Mean (SD)
Shi et al, 2016 [60]	Guangzhou, China	3203 (M: 1025, F: 2178)	40–75[a] M: 62.4 (6.6) F: 59.8 (5.5)	r-P HPLC	–	–	M: 30.5 (10.5) (n = 909) F: 35.0 (11.3) (n = 1973)	M: 6.00 (1.87) (n = 886) F: 6.25 (1.89) (n = 1915)	M: 23.9 (3.0) F: 23.4 (3.2)

M: Male, F: Female, T: Total, mo: months, yr: year, r-P HPLC: Reverse Phase High Pressure Liquid Chromatography, HIG: High Income Group, MIG: Middle Income Group, LIG: Low Income Group
[a]Age group;
[b]Median (interquartile range);
[c]original data in μg/dl , converted into μmol/L by multiplying 0.02322;
[d]original data in mg/dl, converted into μmol/L by multiplying 23.22;
[e]original data in μg/ml, converted into μmol/L multiply by 2.322;
[f]original data in mg/L, converted into μmol/L by multiplying 2.322;
[g]Standard Deviation (SD) not given.

adipose tissue, liver and skeletal muscle contribute to about 90% of total α-tocopherol in the body [19]. Only 1% of the body α-tocopherol is present in the blood [54] and the amount in the circulation is strongly influenced by circulating lipids. This has led to some authors to express vitamin E levels in terms of α-tocopherol:cholesterol ratio. In the absence of an accepted definition for vitamin E deficiency, various authors have used different cutoffs in their studies. This made it difficult for us to compare studies and draw clear conclusions.

Our results, however, indicate trends showing the influence of age and gender on the serum vitamin E levels in the studied population. A steady and age dependent increase of serum α-tocopherol concentration was seen which can be explained by higher circulating lipid level. The difference in vitamin E status between males and females have also been previously reported by several authors [1, 31, 32, 45, 47] presumably due to physiological differences in lipid absorption, metabolism and storage between both sexes. The same cut off is however, being used till date for defining and comparing the vitamin E status of men and women. Data trends also indicate that children of all ages are most vulnerable to high risk of α-tocopherol deficiency and this may be attributed to poor overall nutritional intake, higher prevalence of other oxidative stressors or genetic predisposition to vitamin E deficiency among Asians [2]. In addition, the use of cut offs equivalent to those in adult population may also have led to over estimation of vitamin E deficiency among children.

Overall this review indicates that vitamin E deficiency is wide spread in the Asian population and has not received lot of scientific attention. Similar findings of vitamin E deficiency (cut off < 12 μmol/L) have also been reported in the Middle East and Africa (27 %) and some Asian countries (16%), followed by America (11%) and Europe (8%) [5]. Using a threshold for serum concentration of 20 μmol/L, 27 % of the Americans, 80 % of the Middle East/Africans, 62 % of the Asians, and 19 % of the Europeans fell below this value [5]. This calls for defining cut off limits as well as assessment of vitamin E deficiency.

This review, however, has a number of potential limitations. Firstly, most studies were conducted in very few countries in Asia, so the results are not representative of the population of the Asian continent. Asia being a biggest and most populous continent, more data is required from other parts of the continent to draw clearer inferences. Secondly, many studies have not reported α-tocopherol: cholesterol ratio which is a more accurate representation of vitamin E status. Finally, the different cut-offs used to describe deficiency, the missing agreement on optimal status in each study and the heterogeneity in results make it very difficult to draw clear conclusions on the extent of vitamin E deficiency in Asia.

Table 4. Vitamin E status in elderly.

Publication	Location	n (Sex)	Age (years) Range/Mean (SD)	Assay method	Definition of deficiency	% Deficiency	Mean (SD) α-Tocopherol (μmol/L)	Mean (SD) α-Tocopherol: total cholesterol (μmol/mmol)	BMI (kg/m^2) Mean (SD)
					(i) α-Tocopherol (μmol/L) Or (ii) α-Tocopherol: total cholesterol (μmol/mmol)				
Sripanidkulchai et al, 2003 [45]	Northeast Thailand	82 (M: 36, F: 46)	>56[a]	HPLC	–	–	T: 24.61 (0.93) M: 22.99 (1.63) F: 26.01 (1.16)	–	–
Suwannalert et al, 2007 [47]	Northeast Thailand	207 (M: 72, F: 185)	60–91[a]	r-P HPLC	–	–	T: 22.10[g] M: 18.96 (0.74) F: 23.78 (0.74)	–	–
Assantachai and Lekhakula, 2007 [48]	Thailand	2336 (M/F)	>60[a] 60–97 years[a] 68.94 (6.76)	HPLC	(i) Deficient < 14.0[c]	55.5%	–	–	22.62 (4.34)
Kang et al, 2004 [32]	Taiwan	362 (M: 186, F: 176)	>65[a]	HPLC	(i) Deficient < 11.6 (ii) Deficient < 1.59 (Tocopherol: cholesterol & TG)	– (ii) M: 0.13% F: 0.84%	M: 20.0 (0.6) F: 26.4 (2.3)	M: 3.35 (0.12) F: 3.66 (0.29)	–
Cheng et al, 2005 [1]	Taiwan	2373 (M: 1196, F: 1177)	>65[a]	r-P HPLC	(i) Normal > 16.28	86.48%		T: 5.84 (0.11) (n = 2349)	–
					Marginal: 11.6–16.28	10.61%	T: 27.12 (0.47)	M: 5.53 (0.08)	
					Deficient < 11.6	2.91%		F: 6.18 (0.15)	
						(i) M: 3.60%	M: 25.07 (0.35)		
						F: 2.17%	F: 29.33 (0.67)		
					(ii) Deficient < 2.8	T: 4.2%			
						(ii) M: 5.32%			
						F: 3.0%			

M: Male, F: Female, T: Total, mo: months, yr: year, R: Rural, U: Urban, r-P HPLC: Reverse Phase High Pressure Liquid Chromatography
[a]Age group;
[b]Median (interquartile range);
[c]original data in μg/dl , converted into μmol/L by multiplying 0.02322;
[d]original data in mg/dl, converted into μmol/L by multiplying 23.22;
[e]original data in μg/ml, converted into μmol/L multiply by 2.322;
[f]original data in mg/L, converted into μmol/L by multiplying 2.322;
[g]Standard Deviation (SD) not given.

In the absence of adequate literature on vitamin E status of Asian population, this review indicates that vitamin E intake via the diet and serum levels in population groups in Asia should be revisited to allow better understanding on its role in public health and strategies to improve the vitamin E status.

References

1. Cheng, W.Y., Fu, M.L., Wen, L.J., Chen, C., Pan, W.H., & Huang, C.J. (2005) Plasma retinol and a-tocopherol status of the Taiwanese elderly population. Asia Pac J Clin Nutr. 14, 256–256.
2. Dror, D.K., & Allen, L.H. (2011) Vitamin E deficiency in developing countries. Food Nutr Bull. 32, 124–143.
3. Shahidi, F., & de Camargo, A.C. (2016) Tocopherols and tocotrienols in common and emerging dietary sources: occurrence, applications, and health benefits. Int J Mol Sci. 17, 1745.
4. Mariotti, C., Gellera, C., Rimoldi, M., Mineri, R., Uzeil, G., Zorzi, G., et al. (2004) Ataxia with isolated vitamin E deficiency: neurological phenotype, clinical follow-up and novel mutations in TTPA gene in Italian families. Neurol Sci. 25, 130–137.
5. Peter, S., Friedel, A., Roos, F., Wyss, A., Eggersdorfer, M., Hoffmann, K., & Weber, P. (2016) A systematic review of global alpha-tocopherol status as assessed by nutritional intake levels and blood serum concentrations. Int J Vitam Nutr Res. 85, 261–281.
6. Meydani, S.N., Meydani, M., Blumberg, J.B., Leka, L.S., Siber, G., Loszewski, R., et al. (1997) Vitamin E supplementation and in vivo immune response in healthy elderly subjects. A randomized controlled trial. JAMA. 277, 1380–1386.
7. Knekt, P., Aromaa, A., Maatela, J., Aaran, R.K., Nikkari, T., Hakama, M., et al. (1988) Serum vitamin E and risk of cancer among Finnish men during a 10 year follow up. Am J Epidemiol. 127, 28–41.
8. Negis, Y., Zingg, J.M., Libinaki, R., Meydani, M., & Azzi, A. (2009) Vitamin E and cancer. Nutr Cancer. 61, 875–878.
9. Cherubini, A., Martin, A., Andres-Lacueva, C., Di Iorio, A., Lamponi, M., Mecocci, P., et al. (2005) Vitamin E levels, cognitive impairment and dementia in older persons: the InCHIANTI study. Neurobiol Aging. 26, 987–994.
10. Hadi, H.E., Vettor, R., & Rossato, M. (2018) Vitamin E as a treatment for nonalcoholic fatty liver disease: reality or myth? Antioxidants. 7, 12.
11. Engelhart, M.J., Geerlings, M.I., Ruitenberg, A., Van Swieten, J. C., Hofman, A., Witteman, J.C., et al. (2002) Dietary intake of antioxidants and risk of Alzheimer disease. JAMA. 287, 3223–3229.
12. Traber, M.G. (2014) Vitamin E inadequacy in humans: causes and consequences. Adv Nutr. 5, 503–514.
13. Lim, Y., & Traber, M.G. (2007) Alpha-Tocopherol Transfer Protein (α-TTP): Insights from alpha-tocopherol transfer protein knockout mice. Nutr Res Pract. 1, 247–253.
14. Traber, M.G., & Manor, D. (2012) Vitamin E. Adv Nutr. 3, 330–1.
15. Balogun, O.O., Da Silva Lopes, K., Ota, E., Takemoto, Y., Rumbold, A., Takegata, M., & Mori, R. (2016) Vitamin supplementation for preventing miscarriage. Cochrane Database Syst Rev.Cd004073.
16. Grey, K.F. (1995) Cardiovascular disease and vitamins. Concurrent correction of 'suboptimal' plasma antioxidant levels may, as important part of 'optimal' nutrition, help to prevent early stages of cardiovascular disease and cancer, respectively. Bibl Nutr Dieta. 52, 75–91.
17. Sanyal, A.J., Chalasani, N., Kowdley, K.V., McCullough, A., Diehl, A.M., Bass, N.M., et al. (2010) Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. N Engl J Med. 362, 1675–1685.
18. Sato, K., Gosho, M., Yamamoto, T., Kobayashi, Y., Ishii, N., Ohashi, T., et al. (2015) Vitamin E has a beneficial effect on nonalcoholic fatty liver disease: a meta-analysis of randomized controlled trials. Nutrition. 31, 923–30.
19. Debier, C., & Larondelle, Y. (2005) Vitamins A and E: metabolism, roles and transfer to offspring. Br J Nutr. 93, 153–175.
20. Institute of Medicine, US. (2000). Panel on Dietary Antioxidants and Related Compounds. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington (DC): National Academies Press (US). Vitamin E. Available from: http://www.ncbi.nlm.nih.gov/books/NBK225461/ (accessed on 15th July 2016)
21. Al Saleh, I., El Doush, I., & Billedo, G. (2007) Age and gender-related reference values for serum dl-alpha-tocopherol and all-trans-retinol levels in Saudi population. Int J Vitam Nutr Res. 77, 326–335.
22. Olmedilla, B., Granado, F., Gil-Martinez, E., Blanco, I., & Rojas-Hidalgo, E. (1997) Reference values for retinol, tocopherol, and main carotenoids in serum of control and insulin-dependent diabetic Spanish subjects. Clin Chem. 43, 1066–1071.
23. Ford, L., Farr, J., Morris, P., & Berg, J. (2006) The value of measuring serum cholesterol-adjusted vitamin E in routine practice. Ann Clin Biochem. 43, 130–134.
24. Gibson, R. (2005). Principles of Nutritional Assessment (2nd ed.). New York, NY: Oxford University Press.
25. Thurnham, D.I., Davies, J.A., Crump, B.J., Situnayake, R.D., & Davis, M. (1986) The use of different lipids to express serum tocopherol: lipid ratios for the measurement of vitamin E status. Ann Clin Biochem. 23, 514–520.
26. West, K.P. Jr, Cole, R.N., Shrestha, S., Schulze, K.J., Lee, S.E., Betz, J., Nonyane, B.A., Wu, L.S., Yager, J.D., Groopman, J.D., & Christian, P. (2015) A plasma alpha-tocopherome can be identified from proteins associated with vitamin E status in school-aged children of Nepal. J Nutr. 145, 2646–2656.
27. Rizvi, S., Raza, S.T., Ahmed, F., Ahmad, A., Abbas, S., & Mahdi, F. (2014) The role of vitamin E in human health and some diseases. Sultan Qaboos Univ Med J. 14, 157–165.
28. Wang, Y.Z., Ren, W.H., Liao, W.Q., & Zhang, G.Y. (2009) Concentrations of antioxidant vitamins in maternal and cord serum and their effect on birth outcomes. J Nutr Sci Vitaminol (Tokyo). 55, 1–8.
29. Mai, T., Nguyen, K., Kawakami, M., Kawase, M., & Nguyen, C. (2003) Micronutrient status of primary school girls in rural and urban areas of South Vietnam. Asia Pac J Clin Nutr. 12, 178–85.
30. Sirivichayakul, C., Changbumrung, S., Chanthavanich, P., et al. (2001) Plasma retinol and alpha-tocopherol level and growth indices of 7 months old healthy Thai infants in Bangkok. Southeast Asian J Trop Med Public Health. 32, 408–12.
31. Al-Saleh, I., Billedo, G., El-Doush, I., Mohamed, G.E., & Yosef, G. (2006) Selenium and vitamins status in Saudi children. Clin Chim Acta. 368, 99–109.
32. Kang, M.J., Lin, Y.C., Yeh, W.H., & Pan, W.H. (2004) Vitamin E status and its dietary determinants in Taiwanese–results of the Nutrition and Health Survey in Taiwan 1993–1996. Eur J Nutr. 43, 86–92.
33. Giraud, D.W., Kim, Y.N., Cho, Y.O., & Driskell, J.A. (2008) Vitamin E inadequacy observed in a group of 2- to 6-year-old

children living in Kwangju, Republic of Korea. Int J Vitam Nutr Res. 78, 148–55.
34. Asemi, Z., Taghizadeh, M., Sarahroodi, S., Jazayeri, S., Tabasi, Z., & Seyyedi, F. (2010) Assessment of the relationship of vitamin D with serum antioxidant vitamins E and A and their deficiencies in Iranian pregnant women. Saudi Med J. 31, 1119–23.
35. Shamim, A.A., Schulze, K., Merrill, R.D., et al. (2015) First-trimester plasma tocopherols are associated with risk of miscarriage in rural Bangladesh. Am J Clin Nutr. 101, 294–301.
36. Jiang, T., Christian, P., Khatry, S.K., Wu, L., & West, K.P. Jr (2005) Micronutrient deficiencies in early pregnancy are common, concurrent, and vary by season among rural Nepali pregnant women. J Nutr. 135, 1106–12.
37. Shamim, A.A., Kabir, A., Merrill, R.D., et al. (2013) Plasma zinc, vitamin B(12) and α-tocopherol are positively and plasma γ-tocopherol is negatively associated with Hb concentration in early pregnancy in north-west Bangladesh. Public Health Nutr. 16, 1354–1361.
38. Hammouda, S.A., Abd Al-Halim, O.A., & Mohamadin, A.M. (2013) Serum levels of some micronutrients and congenital malformations: a prospective cohort study in healthy saudi-arabian first-trimester pregnant women. Int J Vitam Nutr Res. 83, 346–54.
39. Andert, C.U., Sanchaisuriya, P., Sanchaisuriya, K., Schelp, F.P., & Schweigert, F.J. (2006) Nutritional status of pregnant women in Northeast Thailand. Asia Pac J Clin Nutr. 15, 329–34.
40. Kim, Y.N., & Cho, Y.O. (2015) Vitamin E status of 20- to 59-year-old adults living in the Seoul metropolitan area of South Korea. Nutr Res Pract. 9, 192–198.
41. Hiraoka, M. (2001) Nutritional status of vitamin A, E, C, B1, B2, B6, nicotinic acid, B12, folate, and beta-carotene in young women. J Nutr Sci Vitaminol (Tokyo). 47, 20–27.
42. Kieu, N.T., Yurie, K., Hung, N.T., Yamamoto, S., & Chuyen, N.V. (2002) Simultaneous analysis of retinol, beta-carotene and tocopherol levels in serum of Vietnamese populations with different incomes. Asia Pac J Clin Nutr. 11, 92–97.
43. Abiaka, C., Al-Tobi, M., & Joshi, R. (2008) Serum micronutrient and micromineral concentrations and ratios in healthy Omani subjects. Med Princ Pract. 17, 334–339.
44. Abiaka, C., Olusi, S., & Simbeye, A. (2002) Serum concentrations of micronutrient antioxidants in an adult Arab population. Asia Pac J Clin Nutr. 11, 22–27.
45. Sripanidkulchai, B., Vaikrutta, S., Sriamporn, S., et al. (2003) Serum antioxidant vitamin levels of people in Khon Kaen, northeastern Thailand. Asian Pac J Cancer Prev. 4, 147–52.
46. Obeid, O.A., Al-Ghali, R.M., Khogali, M., & Hwalla, N. (2006) Vitamins A and E status in an urban Lebanese population: a case study at Dar Al-Fatwa area, Beirut. Int J Vitam Nutr Res. 76, 3–8.
47. Suwannalert, P., Boonsiri, P., Khampitak, T., Khampitak, K., Sriboonlue, P., & Yongvanit, P. (2007) The levels of lycopene, alpha-tocopherol and a marker of oxidative stress in healthy northeast Thai elderly. Asia Pac J Clin Nutr. 16, 27–30.
48. Assantachai, P., & Lekhakula, S. (2007) Epidemiological survey of vitamin deficiencies in older Thai adults: implications for national policy planning. Public Health Nutr. 10, 65–70.
49. Borel, P., Preveraud, D., & Desmarchelier, C. (2013) Bioavailability of vitamin E in humans: an update. Nutr Rev. 71, 319–331.
50. Reboul, E. (2017) Vitamin E bioavailability: mechanisms of intestinal absorption in the spotlight. Antioxidants (Basel). 6, 95.
51. Schmolz, L., Birringer, M., Lorkowski, S., & Wallert, M. (2016) Complexity of vitamin E metabolism. World J Biol Chem. 7, 14–43.
52. Clarke, M.W., Burnett, J.R., & Croft, K.D. (2008) Vitamin E in human health and disease. Crit Rev Clin Lab Sci. 45, 417–50.
53. Aparicio, J.M., Belanger-Quintana, A., Suarez, L., et al. (2001) Ataxia with isolated vitamin E deficiency: case report and review of the literature. J Pediatr Gastroenterol Nutr. 33, 206–210.
54. Horwitt, M.K., Harvey, C.C., Dahm, C.H., & Searcy, M.T. (1972) Relationship between tocopherol and serum lipid levels for the determination of nutritional adequacy. Ann NY Acad Sci. 203, 223–236.
55. Ulak, M., Chandyo, R.K., Thorne-Lyman, A.L., et al. (2016) Vitamin status among breastfed infants in Bhaktapur, Nepal. Nutrients. 8, 149.
56. Schulze, K.L., Christian, P., Wu, L.S., et al. (2014) Micronutrient deficiencies are common in 6- to 8-year-old children of rural Nepal, with prevalence estimates modestly affected by inflammation. J Nutr. 144, 979–987.
57. Al-Saleh, I., El-Doush, I., Billedo, G., Mohamed Gel, D., & Yosef, G. (2007) Status of selenium, vitamin E, and vitamin A among Saudi adults: potential links with common endemic diseases. J Environ Pathol Toxicol Oncol. 26, 221–43.
58. Boonsiri, P., Pooart, J., Tangrassameeprasert, R., & Hongsprabhas, P. (2007) Serum beta-carotene, lycopene and alpha-tocopherol levels of healthy people in northeast Thailand. Asia Pac J Clin Nutr. 16, 47–51.
59. Zou, Y., Wang, D.H., Sakano, N., et al. (2014) Associations of serum retinol, alpha-tocopherol, and gamma-tocopherol with biomarkers among healthy Japanese men. Int J Environ Res Public Health. 11, 1647–60.
60. Shi, W.Q., Liu, J., Cao, Y., Zhu, Y.Y., Guan, K., & Chen, Y.M. (2016) Association of dietary and serum vitamin E with bone mineral density in middle-aged and elderly Chinese adults: a cross-sectional study. Br J Nutr. 115, 113–20.

History
Received April 15, 2018
Accepted September 7, 2018
Published online May 24, 2019

Acknowledgments
All the authors have contributed to the content of manuscript.

Conflict of interest
The authors declare no conflict of interest.

Geeta Trilok-Kumar
Director
Institute of Home Economics
University of Delhi
Delhi
India
Tel: +911146018108
Fax: +911126510711

geetatrilokkumar@gmail.com