Nutrición Hospitalaria

Nutr Hosp. 2011;26(2):280-288
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Revisión

Retinol, β-carotene, α-tocopherol and vitamin D status in European adolescents; regional differences and variability: A review

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Abstract

Currently, blood levels to define vitamin deficiency or optimal status in adolescents are extrapolated from adults. This may be not adequate as vitamin requirements during adolescence depend on the process of sexual maturation, rapid increasing height and weight, among other factors. In order to establish the state of the art, Medline database (www.ncvi.nlm.nih.gov) was searched for studies published in Europe between 1981 and 2010 related to liposoluble vitamin status in adolescents. A comparison of the vitamin status published in the reviewed articles was difficult due to the lack of studies, lack of consensus on cut-off levels indicating deficiency and optimal vitamin levels and the different age-ranges used. In spite of that, deficiency prevalence varied for vitamin D (13-72%), vitamin A (3%), E (25%) and β-carotene (14-19%). Additional factors were considered as possible determinants. We conclude that it is necessary to establish a consensus on acceptable ranges and cut-offs of these vitamins during adolescence. Representative data are still missing; therefore, there is a high need to get deeper into the investigation on liposoluble vitamins in this population group.

(*Nutr Hosp.* 2011;26:280-288)

DOI:10.3305/nh.2011.26.2.4971

Key words: *Vitamins. Adolescence. Nutritional status. Risk factors.*

ESTADO DE RETINOL, β-CAROTENO, α-TOCOPHEROL Y VITAMINA D EN ADOLESCENTES EUROPEOS; DIFERENCIAS REGIONALES Y VARIABILIDAD: REVISIÓN

Resumen

En la actualidad, los diferentes valores sanguíneos que definen un estado óptimo o deficiente de vitaminas liposolubles en los adolescentes son extrapolados de los adultos. Sin embargo, podría no ser lo adecuado debido a que los requerimientos vitamínicos de los adolescentes están marcados por el proceso de maduración sexual y crecimiento entre otros factores. Para establecer el punto de partida, la base de datos Medline (www.ncvi.nlm.nih.gov) ha sido el medio utilizado para la búsqueda de los estudios publicados sobre el estado en vitaminas liposolubles en adolescentes europeos entre los años 1981 y 2010. Comparar los diferentes resultados obtenidos en los diferentes estudios fue difícil debido a la carencia de estudios, a la falta de consenso en los puntos de corte que indican deficiencia y estado óptimo y a los diferentes rangos de edad utilizados. A pesar de esto, en función de los estudios, se observa una variabilidad en la prevalencia de deficiencia de vitamina D (13-72%), vitamina A (3%), E (25%) y β-caroteno (14-19%). Otros factores adicionales fueron considerados como posibles determinantes del estado vitamínico. Se identifica la necesidad de establecer un consenso sobre los rangos aceptables y puntos de corte de estas vitaminas para este grupo de población y profundizar en la investigación de las vitaminas liposolubles en el periodo de la adolescencia.

(*Nutr Hosp.* 2011;26:280-288)

DOI:10.3305/nh.2011.26.2.4971

Palabras clave: *Vitaminas. Adolescencia. Estado nutricional. Factores de riesgo.*

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Recibido: 24-VI-2010.
1.ª Revisión: 14-IX-2010.
Aceptado: 17-IX-2010.

Abbreviations

BMI: Body Mass Index.
RBP: Retinol Binding Protein.

Introduction

Vitamin deficiency, at least on a subclinical level, could be an unrecognized health problem in children and adolescents in Europe because they are not routinely screened for in these population groups. Especially adolescents are considered as a risk group for malnutrition because of their increasing needs in nutrients and energy intake for an adequate growth and development varying with age.[1] Additionally to that, the risk for malnutrition is enhanced because although the access to high quality food and nutrition is continuously improving in European countries,[2] dietary patterns and food choices are not optimal and not according to recommended guidelines.[1]

Vitamins are specifically involved in multiple cellular and tissue processes,[3] and there is increasing evidence that links deficiencies with chronic diseases like cardiovascular and cerebrovascular disease, cancer, diabetes and osteoporosis in adulthood,[1-8] though data are scarce for younger ages. But deficiency stages at these early ages could contribute to risk factors,[2,5,8-10] beside other already described implications like higher risk for osteomalacia,[8,11,12] impaired cognitive function and concentration problems,[13,14] hyperactivity[9] and immune system impairment.[8,13,15] For identifying deficiency stages, reference values are currently extrapolated from adult data for most vitamins.[16]

As already mentioned, little information exists on the vitamin status of representative populations in European countries, particularly for Eastern Europe. Lambert et al. published a review on the contribution of essential nutrients and nutritional status of European adolescents, but vitamins were barely mentioned.[17] Complementary to that review, we published a review on B vitamin status in European adolescents some years ago.[18] The aim of the present review is to get more information about the existing data to give a better overview on fat soluble vitamin (A, E, D and provitamin β-carotene) status in European adolescents, with a specific focus on blood levels, reference values and assessment methods.

Material and methods

Those studies which evaluated blood fat soluble vitamin levels in European adolescents were included in this review. The database Medline (www.ncvi.nlm.nih.gov) was used for searching studies published between 1981 and 2010. Terms like "European adolescents", "liposoluble or fat soluble vitamins", "vitamin status and values", "antioxidants", names of European countries and technical terms of the different liposoluble vitamins as well as combinations out of these terms were entered in the data base for the search. In addition, references of relevant articles were also used to get further information. Because the adolescence period goes from childhood to adulthood, age ranges vary in different articles and data for a broader age-range had to be included (from 9 to 18 years).

Results

A total of 17 articles including around 4503 subjects from different European countries were found focused on the assessment of liposoluble vitamins in adolescents, from North (Finland, Sweden, Ireland, Poland and Denmark), East (Yugoslavia, Austria and Hungary), West (France and Great Britain) and South (Italy and Greece) Europe. Analysing the number of subjects, only three studies included a sample size of less than 50 persons. Two studies analysed a population between 50-100, seven between 100 and 500 and four studies between 500 and 1,000 subjects (table I).

Vitamin D status in European adolescents

The main sources of vitamin D are subcutaneous skin synthesis under the influence of ultraviolet light (290-315 nm) and food.[19] Vitamin D deficiency has been identified as a common problem in Europe.[19-21] Due to the geographical situation of our continent, located at high latitude of 40º N in Madrid (Spain) and 60º N in Oslo (Norway), the skin synthesis of vitamin D may not compensate a low nutritional intake. Moreover, vitamin D intake in Europe is in general low (≤ 2-3 mg/d)[21]. In all the reviewed studies vitamin D status was assessed by means of serum 25-hydroxycholecalciferol [25(OH)D], which is the main circulating vitamin D metabolite, representing not only the consumed amount through diet and supplements but also the subcutaneous synthesis.[19,22,23] One of the most important applications of vitamin D assessment in adolescence is the determination of abnormal serum concentrations of calcium for bone health. Moderately low levels of vitamin D may have adverse effects on calcium homeostasis leading to bone loss, even without symptoms of osteomalacia.[19,24,28] Some studies report a positive association between serum [25(OH)D] and bone mineral content in adolescents.[25,26] Inadequate vitamin D levels have been related to other diseases such as diabetes, multiple sclerosis and cancer.[27,28]

Even vitamin D reference values for deficiency have been set at 27.5 nmol/L in children,[16] there is still a lack of consensus on the deficient and sufficient 25(OH)D concentration, that varies from 20 nmol/L to 100 nmol/L in studies. A proposed scale for the adult population defined hypovitaminosis D as 25(OH)D concentrations below 100 nmol/L, insufficient vitamin D at

Table I
Studies on the nutritional status of fat-soluble vitamins in adolescents

	Country	Year	Author	Subjects			Vitamins	Additional parameters
				Age (years)	Gender	N.º of subjects		
North	Finland	1997	Lehtonen-Veromaa et al. (1999)[20]	9-15	♀	191	D	
	Sweden	N.D.	Drott et al. (1993)[51]	12-13, 13-14, 14-15, 15-16	♂,♀	35	A, E	RBP
	Irland, Finland, Poland, Denmark	2002/03	Andersen R et al. (2005)[36]	12-13	♀	199	D	
East	Yugoslavia	N.D.	Buzina et al.(1982)[50]	12-15		201	A	
	Slovaquia	N.D.	Krajcovicova et al. (1997)[54]	11-14	♂,♀	58	A, E	β-C
	Hungary	N.D.	Molnar et al.(2004)[40]	13-16	♂,♀	48	A, E	β-C
	Austria	1991	König y Elmadfa (2000)[35]. ASNS	10-12, 13-14, 15-19	♂,♀	980	D	
	Austria	1991	Elmadfa et al. (1994)[15]. ASNS	10-12,13-14, 15-18	♂,♀	N.D.	A, E, K	
	Austria	N.D	Marktl et al. (1982)[52]	11-12	♂,♀	797	A, E	
West	France	N.D.	Guillemant et al. (2001)[4]	13-16	♂	54	D	
	France	1988	Hercberg et al. (1994)[50]	10-14,14-18	♂,♀	108	A, E	β-C, VitE/Chol
	France	1988/89	Herbeth et al. (1991)[43]	10-15	♂,♀	509	A, E	β-C
	France	1985/6	Malvy et al. (1993)[56]	12-13,14-16	♂,♀	211	A, E	RBC; β-C, VitE/Chol
	France	1985/86	Malvy et al. (1989)[47]	9-12,12-14,14-16	♂,♀	251	A, E	β-C, VitE/Chol
	Great Britain	1997	Gregory et al. (2000)[37]	11-14,15-18	♂,♀	656	D, A, E	ß-C, VitE/Chol
South	Greece	N.D.	Hassapidou et al. (1996)[55]	13-14	♂,♀	20	E	
	Italy	N.D.	Bonofiglio et al. (1999)[38]	11-16	♀	185	D	

N.D.: Not documented; β-C: β-carotene; ASNS: Austrian Study on Nutritional Status of Schoolchildren.

concentrations of 25(OH)D below 50 nmol/L and a vitamin D deficiency when values are below 25 nmol/L.[29] The German, Swiss and Austrian Nutrition societies (D-A-CH) also agree to the latter data, that serum 25(OH)D levels between 20 to 25 nmol/L present a suboptimal state.[16,30] There is a consensus that serum 25(OH)D concentrations below 10 nmol/L lead to risk of rickets, osteomalacia, increase in cardiovascular and cancer risk factors among others.[8,24,31-34]

Several factors can influence vitamin D status. Regional differences can be appreciated throughout Europe (table II). The highest values for vitamin D were found in French teenagers,[4] the lowest values were found in an Austrian study.[35] Depending on the cut offs used (varying from 15 nmol/L to 25 nmol/l), vitamin D deficiency ranged from 13 to 72% due to geographical differences.

Seasonal differences have been studied by several authors.[4,20,36,37] In both French and Austrian children significant differences in serum concentrations between summer and winter were found, showing higher concentrations in summer.[4,37] The prevalence of suboptimal vitamin D status was 5% lower in summer due to more adequate sun exposure in Finnish children.[20]

The influence of age and Tanner stage on vitamin D status was analyzed in several studies with a significant decrease in concentrations of 25(OH)D levels with increasing age in both sexes ($p < 0.05$),[35,37] although in British children aged 15 and above some slight increases were observed. Contrary to that, Bonofiglio et al. found a significant higher concentration of 25(OH)D in Italian postmenarcheal girls compared to premenarcheal ones ($p < 0.01$).[38] This could be due to the higher concentrations of vitamin D binding protein caused by the increase of estrogens levels.

The influence of body composition on vitamin D levels was studied by Smotkin-Tangorra et al.,[39] who found an inverse correlation between 25(OH)D levels and body mass index (BMI). Regarding supplementation, Guillemant et al.[4] and Lehtonen-Veromaa et al.[20] observed a significant effect on 25(OH)D serum levels ($p = 0.000$) in French and Finnish children (table II).

A, E and provitamin β-carotene vitamin status in European adolescents

Vitamin E and the provitamin β-carotene have an important role as antioxidants in the human body.[40] Current lifestyle of adolescents with a low intake of fruits and vegetables[17,41] could create a pro-oxidant situation with serious long-term consequences. Also vitamin A during adolescence is critical due to its role in cell growth, vision and tissue development. High oxidative stress and free radical levels are involved in the development of cardiovascular disease and other undesirable metabolic situations in adulthood,[40,41] but risk factors are already established during childhood and adolescence.[42]

Little is known about the reference blood levels of these vitamins during adolescence.[43] In adults, the World Health Organization (WHO) defines a defi-

Table II
Vitamin D status

Age (years) / *Authors*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*	*19*
Lehtonen-Veromaa et al.[20] *Finland*	♀ (1)[1] 33.9 ± 13.9 nmol/l ♀ (2)[1] 62.9 ± 15.0 nmol/l (summer) ♀ (3)[1] 33.7 ± 11.4 nmol/l										
Guillemant et al.[4] *France*					♂ (1)[1] 71.6 ± 19.9 nmol/l (summer) ♂ (2)[1] 20.4 ± 6.9 nmol/l (winter) ♂ (3)[1] 52.4 ± 16.3 nmol/l (summer) ♂ (4)[1] 21.4 ± 6.1 nmol/l (winter)						
König y Elmadfa[35] *Austria*		9.9 ± 6.1 nmol/l			9.2 ± 6.9 nmol/l		11.2 ± 8.1 nmol/l				
Gregory et al.[37] *Great Britain*			♂ 56.7 ± 24.05 nmol/l ♀ 54.4 ± 23.52 nmol/l				♂ 56.7 ± 24.05 nmol/l ♀ 54.4 ± 23.52 nmol/l				
Bonofiglio et al.[38] *Italy*			♀ 17.9 ± 1.1 ng/ml[2] ♀ 44.75 ± 2.75 nmol/l[2+3] ♀ 23.2 ± 0.7 ng/ml[4] ♀ 58 ± 1.75 nmol/l[4+3]								
Andersen R et al.[36] *North of Europe*				♀ 29.4 (20.3, 38.3) nmol/l							

Serum concentrations of 25(OH)D Mean ± SD o Mean (interquartils).
[1]blood extraction number. [2]premenarcheal group. [3]1 nmol/l = 0.4 ng/ml. [4]postmenarcheal group.

ciency of vitamin A through plasma retinol values.[44] Concentrations lower than 10 μg/dL (0.35 μmol/L) indicate a deficiency and values between 10 and 20 μg/dL (0.7 μmol/L) are referred to as incipient deficiency.[45]

Beta-carotene plasma levels are considered as a good indicator for fruit and vegetable consumption, with great importance because of its antioxidant power. Low levels are correlating with a higher risk of chronic diseases.[46] Although plasma values above 0.3 μmol/L are considered as acceptable in adults, β-carotene plasma levels above 0.5 μmol/L seem to have the best preventing effects.[45] To determine the nutritional status of vitamin E the level of serum α-tocopherol is normally used.[45] A strong correlation between total blood fat (triglycerides), cholesterol and α-tocopherol concentration in plasma has been found.[47]

According to D-A-CH the normal α-tocopherol serum concentration for adults is between 12 and 46 μmol/L,[30] but for adolescents there are no explicit values. Although the limit value for an adequate nutritional status is defined between 10-16 μmol/L,[48] the guide value for primary prevention of cardiovascular disease and cancer is higher than 30 μmol/L.[30]

Data on vitamin A, E and β-carotene serum levels from existing European studies are presented in tables III-V. Deficiency states vary between less than 3% for vitamin A,[9,15,49-50] 25% for β-carotene and 14-19% for α-tocopherol.[9,15,50]

Gender seems to have no influence on serum blood levels. Regarding age, differences have been observed. In several studies, vitamin A and Retinol Binding Protein (RBP) levels increased according to age until puberty, where they reached adult levels.[37,47,50,51] Plasma β-carotene and α-tocopherol levels seemed to be more stable through the age span in French children and adolescents.[47,50,51] In British children, β-carotene levels increased with age in both sexes ($p < 0.01$).[37] And Winklhofer-Roob et al.[41] found that age was a significant predictor of plasma α-tocopherol concentration in Swiss subjects aged 0.4 to 38.7 years. Assessing vita-

Table III
Vitamin A status

Age (years) / *Authors*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*
Drott et al.[51] *Sweden*				429 μg/l (211-599)[1] 1.5 μmol/l (0.74-2.10)[4]	924 μg/l (255-1,463)[1] 3,23 μmol/l (0.89-5.12)[4]	670 μg/l (343-1,112)[1] 2,34 μmol/l (1.20-3.90)[4]	576 μg/l (410-805)[1] 2,01 μmol/l (1.43-2.81)[4]			
Buzina et al.[50] *Yugoslavia*				♂: 34.5 ± 8.8 μg/dl[2] 1.21 ± 0.31 μmol/l[4]						
Krajcovicova et al.[54] *Slovaquia*			Vegetarians: 1.91 ± 0.02 μmol/l[2] Omnivores: 1.54 ± 0.07 μmol/l[2]							
Molnar et al.[40] *Hungary*							Normal-weighted: 1.87 ± 0.51 μmol/l[2]			
		Obese: 1.8 ± 0.51 μmol/l[2]								
Hercberg et al.[50] *France*		♂: 1.32 μmol/l (0.73/1.98)[3] ♀: 1.37 μmol/l (0.95/1.89)[3]				♂: 1.56 μmol/l (1.16/2.30)[3] ♀: 1.6 μmol/l (1.27/2.59)[3]				
Malvy et al.[47] *France*	40.3 ± 9.4 μg/dl[2] 1.41 ± 0.33 μmol/l[4]			43.7 ± 9.8 μg/dl[2] 1.53 ± 0.34 μmol/l[4]		51.7 ± 12.2 μg/dl[2] 1.81 ± 0.43 μmol/l[4]				
Malvy et al.[56] *France*				♂: 44.30 μg/dl (28.4-66.4)[1] 1.55 μmol/l (1.0-2.32)[4] ♀: 42.15 μg/dl (21.8-64.0)[1] 1.47 μmol/l (0.76-2.24)[4]		♂: 51.50 μg/dl (25.4-88.7)[1] 1,80 μmol/l (0.9-3.10)[4] ♀: 45.90 μg/dl (33.1-83.2)[1] 1.60 μmol/l (1.16-2.90)[4]				
Elmadfa et al.[15] *Austria*		31.6 ± 7.2 μg/dl[2] 1.10 ± 0.25 μmol/l[4]			33.5 ± 6.3 μg/dl[2] 1.17 ± 0.22 μmol/l[4]		38.6 ± 10.2 μg/dl[2] 1.35 ± 0.36 μmol/l[4]			
Marktl et al.[53] *Austria*			♂: 156 ± 27.9 UI/dl[2] 1.62 ± 0.30 μmol/l[4+5] ♀: 158 ± 26.3 UI/dl[2] 1.66 ± 0.27 μmol/l[4+5]							
Gregory et al.[37] *Great Britain*			♂: 1.27 ± 0.27 μmol/l[2] ♀: 1.37 ± 0.285 μmol/l[2]				♂: 1.53 ± 0.392 μmol/l[2] ♀: 1.51 ± 0.389 μmol/l[2]			

Retinol Plasmatic concentrations.
[1]Median (Range). [2]Mean ± SD. [3]Mean (Percentil 5/Percentil 95). [4]1 μmol/l = 28.6 μg/dl. [5]1 UI = 0.3 g.

Table IV
β-carotene status

Age (years) / *Authors*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*
Krajcovicova et al.[54] *Slovaquia*			Vegetarian: 0.46 ± 0.03 μmol/l[2] Omnivores: 0.26 ± 0.02 μmol/l[2]							
Molnar et al.[40] *Hungary*							Normal-weighted: 0.4 ± 0.304 μmol/l[2]			
				Obese: 0.26 ± 0.112 μmol/l[2]						
Hercberg et al.[50] *France*		♂: 0.64 μmol/l (0.22/1.79)[3] ♀: 0.58 μmol/l (0.17/1.44)[3]				♂: 0.60 μmol/l (0.25/1.85)[3] ♀: 0.60 μmol/l (0.18/2.65)[3]				
Malvy et al.[47] *France*	499 ± 276 μg/l[2] 0.93 ± 0.46 μmol/l[4]			626 ± 388 μg/l[2] 1.17 ± 0.72 μmol/l[4]		525 ± 304 μg/l[2] 0.98 ± 0.57 μmol/l[4]				
Malvy et al.[56] *France*			♂: 480 μg/l (135-1,250)[1] 0.89 μmol/l (0.25-2.33)[4] ♀: 527 μg/l (153-1,405)[1] 0.98 μmol/l (0.29-2.62)[4]			♂: 487 μg/l (335-1,465)[1] 0.91 μmol/l (0.62-2.73)[4] ♀: 442 μg/l (210-1,310)[1] 0.82 μmol/l (0.39-2.44)[4]				
Elmadfa et al.[15] *Austria*		33.2 ± 18.6 μg/dl[2] 0.62 ± 0.35 μmol/l[4]			33.7 ± 20.8 μg/dl[2] 0.63 ± 0.39 μmol/l[4]		40.8 ± 29.6 μg/dl[2] 0.76 ± 0.55 μmol/l[4]			
Marktl et al.[52] *Austria*			♂: 32.2 ± 21.9 μg/dl[2] 0.60 ± 0.41 μmol/l[4] ♀: 25.3 ± 21.6 μg/dl[2] 0.47 ± 0.40 μmol/l[4]							
Gregory et al.[37] *Great Britain*			♂: 0.297 ± 0.2108 μmol/l[2] ♀: 0.272 ± 0.2370 μmol/l[2]				♂: 0.249 ± 0.1781 μmol/l[2] ♀: 0.257 ± 0.1580 μmol/l[2]			

β-carotene plasmatic concentrations.
[1]Median (Range). [2]Mean ± SD. [3]Mean (Percentil 5/Percentil 95). [4]1 μmol/l = 536 μg/l.

mins by pubertal development, a positive correlation was found with vitamin A ($p < 0.001$), and a negative correlation with β-carotene and α-tocopherol serum levels with increasing Tanner stage ($p < 0.05$).[43]

Differences in vitamin status have also been observed in relationship to BMI. In the study by Marktl et al.,[52] obese adolescents presented higher vitamin A levels than normal-weighted. In the study by Molnar et al[40], over-weighted adolescents with metabolic syndrome presented lower values of α-tocopherol and β-carotene than normal weighted ones ($p < 0.01$). However, in over-weighted adolescents without metabolic syndrome, only β-carotene concentrations were significantly lower compared to normal-weighted ones.

The effect of smoking on antioxidant status was studied in Britain by Crawley et al.[53] showing that teenage smokers had a lower intake of antioxidant nutrients, fruits, vegetables and cereals, being particularly significant among girls, but no blood levels were reported. An opposite effect was found among vegetarian subjects that presented higher levels of vitamin A, α-tocopherol and β-carotene than omnivore ones ($p < 0.001$).[54]

In the same way as for vitamin D, seasonal differences have been observed in plasma α-tocopherol, cholesterol and retinol concentrations higher in winter than in the other seasons[41]. In regard to regional differences increased α-tocopherol values were observed in South Europe.[55]

Relationship between the different vitamins has also been studied. Serum retinol had a positive correlation with β-carotene and α-tocopherol levels[37,47,56] and the latter with cholesterol.[43,47,56] Drott et al. on the contrary found an inverse relationship between vitamin A and vitamin E serum concentrations.[51]

The influence of socioeconomic status has been studied by Marktl et al.[52]. Higher β-carotene and vitamin E serum concentrations were found in children of central Europe whose parents had a high socioeconomic background.

General discussion

There are very few published studies on nutritional vitamin status in European adolescents and data are not available for all countries, especially in the eastern part of Europe. Moreover, the percentage of representative studies is low and in some countries the sample is not representative at all of the general population. A comparison of the vitamin status published in the reviewed articles is difficult due to the lack of consensus on cut-

Table V
α-tocoferol status

Age (years) / *Authors*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*
Drott et al.[51] *Sweden*				9.1 mg/l (3.2-13.2)[1] 21.16 µmol/l (7.4-30.7)[4]	6.1 mg/l (2.9-9.7)[1] 14.9 µmol/l (6.7-22.5)[4]	8.2 mg/l (3.0-13.2)[1] 19.07 µmol/l (7.0-30.7)[4]	7.5 mg/l (5.3-10.2)[1] 17.44 µmol/l (12.3-23.7)[4]			
Krajcovicova et al.[54] *Slovaquia*			Vegetarians: 29.17 ± 0.96 µmol/l[2] Omnivores: 22.94 ± 0.62 µmol/l[2]							
Molnar et al.[40] *Hungary*							Normal-weighted: 29.17 ± 0.96 µmol/l[2]			
				Obese: 17.1 ± 4.65 µmol/l[2]						
Hercberg et al.[50] *France*		♂: 18.3 µmol/l (13.4/24.1)[3] ♀: 20.5 µmol/l (14.7/25.9)[3]				♂: 18.3 µmol/l (13.4/24.1)[3] ♀: 20.5 µmol/l (14.7/25.9)[3]				
Malvy et al.[47] *France*	10.0 ± 2.0 mg/l[2] 23.25 ± 4.65 µmol/l[4]			9.7 ± 2.5 mg/l[2] 22.65 ± 5.81 µmol/l[4]		10.0 ± 2.1 mg/l[2] 23.72 ± 4.88 µmol/l[4]				
Malvy et al.[56] *France*				♂: 8.30 mg/l (6.8-13.1)[1] 19.30 µmol/l (15.81-30.46)[4] ♀: 8.9 mg/l (1.1-12.2)[1] 20.7 µmol/l (2.56-28.37)[4]		♂: 9.10 mg/l (5.8-15.7)[1] 21.16 µmol/l (13.49-36.51)[4] ♀: 9.40 mg/l (3.7-13.7)[1] 21.86 µmol/l (8.6-31.86)[4]				
Elmadfa et al.[15] *Austria*		0.88 ± 0.21 mg/dl[2] 20.46 ± 4.88 µmol/l[4]			0.85 ± 0.19 mg/dl[2] 19.77 ± 18.37 µmol/l[4]		0.89 ± 0.20 mg/dl[2] 20.7 ± 4.65 µmol/l[4]			
Marktl et al.[52] *Austria*			♂: 1.17 ± 0.23 mg/dl[2] 27.21 ± 5.35 µmol/l[4] ♀: 1.07 ± 0.22 mg/dl[2] 24.88 ± 5.12 µmol/l[4]							
Gregory et al.[37] *Great Britain*			♂: 19.7 ± 4.02 µmol/l[2] ♀: 20.5 ± 3.48 µmol/l[2]				♂: 19.2 ± 3.97 µmol/l[2] ♀: 19.8 ± 3.97 µmol/l[2]			
Hassapidpou et al.[55] *Greece*					0.79 mg/l (0.7-1.02)[1] 18.37 µmol/l (16.28-23.27)[4]					

α-tocoferol serum concentrations.
[1]Median (Range). [2]Mean ± SD. [3]Mean (Percentil 5/Percentil 95). [4]1 µmol/l = 0,43 mg/l.

off levels indicating deficiency and optimal vitamin levels and the different age-ranges used. Also, the way of presenting the results is not uniform, using the mean ± standard deviation (SD) or the largest median plus 5 and 95 percentiles. Its variation is also due to the variety of laboratory methods, lack of standard reference preparations and calibration materials, and shortages of these issues.[32-35]

Regarding the existing data on liposoluble vitamin status of the European adolescents reviewed, a general hypovitaminosis problem was found for vitamin D and β-carotene in both gender. However, one study carried out in the US by Yetley et al. concluded that males have higher vitamin D intakes and 25(OH)D concentrations than females.[57]

There seem to be several factors that influence liposoluble vitamin status; age, season, BMI, smoking or socioeconomic status should be taken into account in future vitamin studies as possible modificators of vitamin status in adolescents. Vitamin D decreases according to age. In the before mentioned US study, hypovitaminosis D (< 27.5 nmol/L) was observed in 1% of infants and children aged < 11 years, 5% of adolescents aged 12-19 years, and 6% of adults aged < 20 years.[58] Serum α-tocopherol was found to increase slightly with age.[58]

Several studies agree that vitamin D status exhibits a seasonal variation with higher values during the summer period.[4,20,25,28] Both serum 25(OH) D concentration[10,59,60] and biomarkers of bone turnover,[61] positively correlate with bone mineral content. PTH concentrations tend to increase during winter[62] being associated with bone absorption,[11,12] that is related with bone mineral content.

Current research also suggests that obese adolescents present states of malnutrition.[63] This means that, despite an excess of body fat, certain nutrients may be at risk.[27] An inverse relation between antioxidant vitamins and vitamin D with BMI[39] has been observed.[64]

Regarding health costs, Grant et al. suggested for Western countries of Europe that the increase in the mean serum 25(OH)D levels up to 40 ng/mL would have a positive impact on the reduction of direct and indirect economic burden of disease. For 2007, the reduction was estimated at € 187,000 million/year.[65]

Due to the low 25(OH)D concentrations, especially during winter months, some researchers emphasize to improve vitamin D intake through supplements.[66] The fortification of food with vitamin D is not common in Europe, without any regulation in some countries, with the exception of some Scandinavian countries. Vitamin D is considered a pharmacological agent for children when the dose is higher than the levels recommended by the Nordic countries of 5 mg/d (200 IU/d) and till now the data about the influence of vitamin D supplementation or fortified foods in children and adolescents is scarce.[67] On the contrary, seasonal vitamin A intake is not so important. The recommendations in some countries like Ireland, Italy and the United Kingdom are lower than the average for all age ranges in men and women, without any significant deficiencies in these countries respect those with higher recommendations (DACH countries and Romania).

Also other behavioural and health aspects should be taken into account in future studies regarding vitamin status in adolescents. The lower intakes of antioxidant nutrients, fruits, vegetables and cereals by the teenage smokers in comparison with non smokers already mentioned agree with those found by Jain et al.[68] who observed an increased oxidative stress and a compromised antioxidant defence system in smokers.[68] Lenders et al.[64] found that concentrations of 25(OH)D were directly correlated with physical activity levels ($p < 0.05$).

Conclusions

Currently, there are no reference values for blood vitamin levels in adolescents. Analysing the available existing data on nutritional status in European adolescents, the comparability of them implies many difficulties due to the lack of data and reference values as well as the lack of consensus on methodological approaches. The importance of transnational studies in order to standardize the procedures and methodologies and the way to express the results to enable comparison should be highlighted.

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