Review Article
Vitamin D Status in Central Europe

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Little published information is available regarding epidemiological data on vitamin D status in the large geographical region of Central Europe (CE). We searched the journal literature with regard to 25(OH)D concentrations among community-dwelling or healthy people living in CE. 25(OH)D concentrations varied by age, season, study sample size, and methodological approach [i.e., 25(OH)D assay used]. Concentrations of 25(OH)D in CE appeared lower than 30 ng/mL, and the magnitude of hypovitaminosis D was similar to that reported in Western Europe. While most of the studies reviewed were cross-sectional studies, a longitudinal study was also included to obtain information on seasonal variability. The longitudinal study reported wintertime 25(OH)D values close to 21–23 ng/mL for all studied age groups, with a significant increase of 25(OH)D in August reaching 42 ng/mL for those aged 0–9 years, but only 21 ng/mL for the elderly aged 80–89 years. The decrease in 25(OH)D with respect to age was attributed to decreased time spent in the sun and decreased vitamin D production efficiency. Based on the literature review on vitamin D status in the CE populations, it can be concluded that 25(OH)D vitamin D levels are on average below the 30 ng/mL level.

1. Introduction

The literature published over the two last decades indicates increasing awareness of vitamin D’s pleiotropic, multidirectional action in the human body. Evidence from large-scale studies contributed to the understanding that vitamin D deficiency may be a significant risk factor for many civilization diseases. There is recognized benefit of vitamin D for bone health based on both observational studies and randomized controlled trials [1]. There is also evidence largely from cross-sectional, ecological, laboratory, and observational studies that vitamin D reduces risk of many types of cancer, cardiovascular disease, diabetes, autoimmune and metabolic disorders, infectious diseases linked to decreased immunity, and even some neuropsychiatric disorders [2–8]. Based on the journal literature for the
nonskeletal effects of vitamin D, it appears that serum 25-hydroxyvitamin D [25(OH)D] concentrations between 30 and 50 ng/mL are associated with significantly reduced risk of such diseases [9–12]. Therefore, a variety of practical and research activities are being undertaken worldwide to evaluate vitamin D deficiency and improve vitamin D status. In Central Europe (CE), researchers representing the region developed recommendations to treat vitamin D deficiency for Poland in 2009 [13] and for Hungary in 2012 [14]. Because of convincing findings showing potential health benefits of vitamin D, investigators in CE focus on determining serum 25-hydroxyvitamin D [25(OH)D] concentrations in the general population and among different risk groups. This interest inspired a conference, “Vitamin D—minimum, maximum, optimum,” held in Warsaw, Poland, on October 19–20, 2012 (http://www.witaminad.waw.pl/). The meeting was organized by the Children’s Memorial Health Institute, Department of Biochemistry, Radioimmunology, and Experimental Medicine, in Warsaw, with 550 attendees from European and non-European countries. The conference sought to establish recommendations on serum 25(OH)D concentrations for Central Europeans. A related goal was to develop an understanding of current serum 25(OH)D normative ranges and of how they vary with respect to such factors as age, sex, and season. The major purpose was to establish guidelines for appropriate vitamin D supplementation for Central Europeans of all ages in order to ensure adequate serum 25(OH)D concentration and, thereby, to guarantee short- and long-term effects, with appropriate safety considerations. The primary conclusion reached by the participants at the Warsaw conference was consensus on optimal (target) serum 25(OH)D concentrations ranging from 30 to 50 ng/mL (75–125 nmol/L). Although no convincing reports indicate adverse health effects of serum 25(OH)D concentrations up to 100 ng/mL (250 nmol/L), few studies show health benefits associated with levels higher than 50 ng/mL.

2. Materials and Methods

This paper reviews the available spectrum of data on serum 25(OH)D concentrations in CE, compared with selected findings from other European countries. We found several articles through advanced searches of the National Library of Medicine's PubMed database and Scopus, using keywords “vitamin D” or “serum 25-hydroxyvitamin D” along with country names or “Europe.” Some of the CE “epidemiologic” studies reported at the vitamin D conference in Warsaw were also included for further analyses. Papers dealing with healthy or community-dwelling people were included in the tables, but people with diseases were not. However, one set of data for patients was given in a separate table because it provided longitudinal data on serum 25(OH)D concentrations throughout the year [15].

3. Results

Tables 1–4 provide explicit comparative information on serum 25(OH)D concentrations in Central European countries as a function of age [16–46], whereas Table 5 gives information as a function of season (monthly intervals) stratified by age for a Hungarian population [15].

3.1. Neonates and Infants. Eight studies in this review reported serum 25(OH)D concentrations for neonates and infants in CE: one from the Czech Republic and seven from Poland (Table 1). Mean serum 25(OH)D concentration among neonates ranged between 7 and 24 ng/mL depending on season. Winter and spring values were low, 7–14 ng/mL, whereas summertime values were better (19–24 ng/mL). Recent Polish studies confirmed the above observations, showing higher summertime than winter/spring mean 25(OH)D concentrations in the umbilical cord: 24.0 ± 8.5 ng/mL versus 13.7 ± 8.2 ng/mL (P < 0.001), respectively [20–22]. Serum 25(OH)D values found in these studies appeared lower than those recommended on the basis of a recent randomized controlled trial of vitamin D supplementation during pregnancy. This study, performed by Hollis and colleagues, demonstrated association between the 25(OH)D level of 40 ng/mL and optimal serum 1,25-dihydroxyvitamin D concentrations [47]. Fortunately, implementing recommendations for neonates to start vitamin D supplementation from the first days after delivery resolved, at least partly, vitamin D deficiency during the first few months of life. As Czech-Kowalska and colleagues showed, supplementing neonates with daily doses of ~550 IU of vitamin D increased serum 25(OH)D to 55 ng/mL at the third month of life [22]. Further, in the group of infants (n = 43) regularly supplemented with a vitamin D dose of ~1160 IU/day at both the 6th and 12th month, 25(OH)D serum concentrations unexpectedly decreased from 40.2 ± 18.8 ng/mL at the 6th month to 32.0 ± 12.7 ng/mL at the 12th month (P < 0.01) [17]. However, reduced daily vitamin D intake expressed in international units/kilogram of body weight may account for the observed decrease in 25(OH)D concentration [23].

3.2. Children and Adolescents. Table 2 shows serum 25(OH)D concentrations in children and adolescents. In Central European countries, wintertime values ranged from 9 ng/mL in Belarus [24] to 23 ng/mL in Hungary [25]; summertime values ranged from 36 to 56 ng/mL. The large winter range may be due to different 25(OH)D assays used, which will be discussed later. In addition, studies with smaller sample size may have been associated with variations in 25(OH)D concentrations due to recruiting people who may not have been representative of the larger population.

3.3. Adults. Table 3 presents serum 25(OH)D concentrations for adults aged 20–60 years. In CE, wintertime 25(OH)D concentrations ranged from 11 ng/mL in Poland to 18 ng/mL in Estonia. Summertime 25(OH)D concentrations ranged from 18 ng/mL in Ukraine to 35 ng/mL in Hungary, and annual values found in larger studies (>100 cases) ranged from 14 ng/mL in Ukraine to 29 ng/mL in Belarus. In Western European countries of similar latitude, wintertime values ranged from 13 ng/mL in Denmark to 20 ng/mL in Austria, whereas those in summertime ranged from 23 to 35 ng/mL.
Table 1: Serum 25-hydroxyvitamin D concentrations reported for neonates and infants. (Mean, range, and standard deviations are shown.)

<table>
<thead>
<tr>
<th>Country</th>
<th>City</th>
<th>Latitude, longitude</th>
<th>Year</th>
<th>Number, sex</th>
<th>Age</th>
<th>Population</th>
<th>Season</th>
<th>Assay, machine (manufacturer)</th>
<th>Serum 25(OH)D (ng/mL)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Czech Republic</td>
<td>Pilzen</td>
<td>49.8° N 13.3° E</td>
<td>April–June 2006</td>
<td>28</td>
<td>Newborn</td>
<td>Term, cross section</td>
<td>Spring</td>
<td>CLIA, Liaison (DiaSorin)</td>
<td>7 (6–13)</td>
<td>[16]</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>20 (17)</td>
<td>Newborn 1 week</td>
<td>Healthy</td>
<td>Annual</td>
<td>CLIA, Liaison (DiaSorin)</td>
<td>15 ± 9</td>
<td>[18]</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>56</td>
<td>Newborn 3 weeks</td>
<td>Healthy</td>
<td>Annual</td>
<td>CLIA, Liaison (DiaSorin)</td>
<td>15 ± 9</td>
<td>[19]</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>76</td>
<td>Newborn cord blood</td>
<td>Healthy</td>
<td>Winter</td>
<td>CLIA, Liaison (DiaSorin)</td>
<td>14 ± 8</td>
<td>[20]</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>40</td>
<td>Newborn cord blood</td>
<td>Healthy</td>
<td>Summer</td>
<td>CLIA, Liaison (DiaSorin)</td>
<td>24 ± 9</td>
<td>[21]</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>15 (15)</td>
<td>2 weeks</td>
<td>Healthy</td>
<td>Winter, summer</td>
<td>CLIA, Liaison (DiaSorin)</td>
<td>8.5 (7–12)</td>
<td>[22]</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>15 (15)</td>
<td>10 weeks</td>
<td>Healthy, after supplementation</td>
<td>Winter, summer</td>
<td>CLIA, Liaison (DiaSorin)</td>
<td>55 (35–67)</td>
<td>[22]</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>134</td>
<td>6 months</td>
<td>Healthy, after supplementation</td>
<td>RIA</td>
<td>43 ± 20</td>
<td>[23]</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>52.2° N 21.0° E</td>
<td>2001-2002</td>
<td>98</td>
<td>12 months</td>
<td>Healthy, after supplementation</td>
<td>RIA</td>
<td>29 ± 12</td>
<td>[23]</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Serum 25-hydroxyvitamin D concentrations reported for children and adolescents.

<table>
<thead>
<tr>
<th>Country</th>
<th>City</th>
<th>Latitude, longitude</th>
<th>Year</th>
<th>Number, sex</th>
<th>Age (yrs)</th>
<th>BMI</th>
<th>Population</th>
<th>Season</th>
<th>Assay, machine (manufacturer)</th>
<th>Serum 25(OH)D (ng/mL)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belarus</td>
<td>Minsk</td>
<td>53.9° N, 27.6° E</td>
<td>2011-2012</td>
<td>47 M</td>
<td>11 (8–13)</td>
<td>Healthy</td>
<td>Autumn-winter</td>
<td>ECLIA, Cobas e411 (Roche Diagnostics)</td>
<td>9 (5–15)</td>
<td>[24]</td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td>Budapest</td>
<td>47.5° N, 17.1° E</td>
<td></td>
<td>100 M</td>
<td>11–14</td>
<td>20</td>
<td>Healthy, Cross section</td>
<td>Winter</td>
<td>CLIA, IDS (IDS)</td>
<td>23 ± 6</td>
<td>[25]</td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
<td></td>
<td></td>
<td>66 M</td>
<td>11–14</td>
<td>20</td>
<td>Healthy</td>
<td>Summer</td>
<td></td>
<td>41 ± 13</td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
<td></td>
<td></td>
<td>91 F</td>
<td>11–14</td>
<td>20</td>
<td>Healthy</td>
<td>Winter</td>
<td></td>
<td>21 ± 8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>53 F</td>
<td>11–14</td>
<td>20</td>
<td>Healthy</td>
<td>Summer</td>
<td></td>
<td>38 ± 14</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td></td>
<td>49–54° N, 15–24° E</td>
<td></td>
<td>199 F</td>
<td>13 ± 1</td>
<td>Community, cross section</td>
<td>Winter</td>
<td>HPLC</td>
<td>12</td>
<td>[26]</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>City</td>
<td>Latitude/longitude</td>
<td>Year</td>
<td>Number</td>
<td>sex</td>
<td>Age (yrs)</td>
<td>BMI</td>
<td>Population</td>
<td>Season</td>
<td>Assay, machine (manufacturer)</td>
<td>Serum 25(OH)D (ng/mL)</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------</td>
<td>--------------------</td>
<td>------------</td>
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<td>------------</td>
<td>---------</td>
<td>-----------------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Belarus</td>
<td>Western Belarus</td>
<td>53°N 24–26°E</td>
<td>2010-2011</td>
<td>6M</td>
<td>22F</td>
<td>46 ± 7</td>
<td>27 ± 4</td>
<td>Healthy</td>
<td>Annual</td>
<td>ECLIA, Elecsys (Roche Diagnostics)</td>
<td>18 ± 7 [28]</td>
</tr>
<tr>
<td>Belarus</td>
<td>Minsk</td>
<td>50.1°N 14.4°E</td>
<td>2011-2012</td>
<td>168F</td>
<td></td>
<td>45–55</td>
<td></td>
<td>Healthy</td>
<td>Annual</td>
<td>ECLIA, Cobas e411 (Roche Diagnostics)</td>
<td>29 ± 15 [29]</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Prague</td>
<td>49.8°N 13.3°E</td>
<td>2004-2006</td>
<td>2175</td>
<td></td>
<td></td>
<td></td>
<td>Clinic patients</td>
<td>Annual</td>
<td>RIA, IDS, UK</td>
<td>31 ± 18 [30]</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Pilzen</td>
<td>59.1°N 26.3°E</td>
<td>2006</td>
<td>167M</td>
<td>32F</td>
<td>53 ± 14</td>
<td>27 ± 5</td>
<td>Community, cross section from patients</td>
<td>Winter</td>
<td>ECLIA, Cobas e411 (Roche Diagnostics)</td>
<td>17 ± 6 [32]</td>
</tr>
<tr>
<td>Estonia</td>
<td>Väike-Maarja</td>
<td>52.2°N 21.0°E</td>
<td>2003-2004</td>
<td>17F</td>
<td>47 (25–79)</td>
<td></td>
<td>Healthy, employees of the Center of Oncology, Opole</td>
<td>November–March</td>
<td>ECLIA, (Roche Diagnostics)</td>
<td>15 ± 8 [20, 21]</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>Warszawa</td>
<td>50.6°N 17.9°E</td>
<td>2003-2004</td>
<td>17F</td>
<td>47 (25–79)</td>
<td></td>
<td>Healthy, employees of the Center of Oncology, Opole</td>
<td>November–March</td>
<td>ECLIA, (Roche Diagnostics)</td>
<td>17 [35]</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>Warszawa</td>
<td>50.6°N 17.9°E</td>
<td>2003-2004</td>
<td>17F</td>
<td>47 (25–79)</td>
<td></td>
<td>Healthy, employees of the Center of Oncology, Opole</td>
<td>November–March</td>
<td>ECLIA, (Roche Diagnostics)</td>
<td>17 [35]</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>Warszawa</td>
<td>50.6°N 17.9°E</td>
<td>2003-2004</td>
<td>17F</td>
<td>47 (25–79)</td>
<td></td>
<td>Healthy, employees of the Center of Oncology, Opole</td>
<td>November–March</td>
<td>ECLIA, (Roche Diagnostics)</td>
<td>17 [35]</td>
<td></td>
</tr>
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</table>

Table 3: Serum 25-hydroxyvitamin D concentrations reported for adults in Central Europe.
Table 3: Continued.

<table>
<thead>
<tr>
<th>Country</th>
<th>City</th>
<th>Latitude, longitude</th>
<th>Year</th>
<th>Number, sex</th>
<th>Age (yrs)</th>
<th>BMI</th>
<th>Population</th>
<th>Season</th>
<th>Assay, machine (manufacturer)</th>
<th>Serum 25(OH)D (ng/mL)</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>55</td>
<td>Pregnant women</td>
<td>Healthy</td>
<td>Annual</td>
<td>23 (17–57)</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>55</td>
<td>Pregnant women</td>
<td>Healthy</td>
<td>Annual</td>
<td>25 (6–53)</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>55</td>
<td>Pregnant women</td>
<td>Healthy</td>
<td>Annual</td>
<td>25 (3–50)</td>
<td>37</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Slovakia</td>
<td></td>
<td>49°N 17–22°E</td>
<td>2007</td>
<td>162F</td>
<td>34</td>
<td>Healthy</td>
<td>October</td>
<td>HPLC</td>
<td>33 ± 13</td>
<td>38</td>
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<tr>
<td>Ukraine</td>
<td></td>
<td>44°27′N–52°2′N</td>
<td>2010-2011</td>
<td>649F</td>
<td>47 (20–59)</td>
<td>28 ± 6</td>
<td>Healthy</td>
<td>Annual</td>
<td>ECLIA, Elecsys 2010 (Roche Diagnostics)</td>
<td>14 ± 9</td>
<td>39, 40</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td>2010-2011</td>
<td>129 M</td>
<td>44 (20–59)</td>
<td>26 ± 6</td>
<td>Healthy</td>
<td>Annual</td>
<td>ECLIA, Elecsys 2010 (Roche Diagnostics)</td>
<td>15 ± 10</td>
<td>39, 40</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td>2010-2011</td>
<td>102 F 28 M</td>
<td>47 ± 10</td>
<td>27 ± 5</td>
<td>Healthy</td>
<td>Winter</td>
<td></td>
<td>13 ± 8</td>
<td>39, 40</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td>2010-2011</td>
<td>160 F 37 M</td>
<td>45 ± 11</td>
<td>27 ± 5</td>
<td>Healthy</td>
<td>Summer</td>
<td></td>
<td>18 ± 10</td>
<td>39, 40</td>
</tr>
</tbody>
</table>
Table 4: Serum 25-hydroxyvitamin D concentrations reported for seniors.

<table>
<thead>
<tr>
<th>Country</th>
<th>City</th>
<th>Latitude, longitude</th>
<th>Year</th>
<th>Number, sex</th>
<th>Age (yrs)</th>
<th>BMI</th>
<th>Population</th>
<th>Season</th>
<th>Assay, machine (manufacturer)</th>
<th>Serum 25(OH)D (ng/mL)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belarus</td>
<td></td>
<td></td>
<td></td>
<td>178 F</td>
<td>65–75</td>
<td></td>
<td></td>
<td>Annual</td>
<td>ECLIA, Cobas e411 (Roche Diagnostics)</td>
<td>26 ± 14</td>
<td>[29]</td>
</tr>
<tr>
<td>Belarus</td>
<td></td>
<td></td>
<td></td>
<td>101 F</td>
<td>&gt;75</td>
<td></td>
<td></td>
<td>Annual</td>
<td></td>
<td>19 ± 9</td>
<td>[29]</td>
</tr>
<tr>
<td>Hungary</td>
<td>Debrecen</td>
<td>47.5° N, 21.6° E</td>
<td>October</td>
<td>319 F</td>
<td>65 (41–91)</td>
<td>26 ± 4</td>
<td>Community</td>
<td>Year</td>
<td>RIA, DiaSorin</td>
<td>19 (5–54)</td>
<td>[43]</td>
</tr>
<tr>
<td>Hungary</td>
<td>Debrecen</td>
<td></td>
<td></td>
<td>100 F</td>
<td>65</td>
<td></td>
<td>Community</td>
<td>Spring</td>
<td></td>
<td>17 (5–40)</td>
<td>[43]</td>
</tr>
<tr>
<td>Hungary</td>
<td>Debrecen</td>
<td></td>
<td></td>
<td>80 F</td>
<td>65</td>
<td></td>
<td>Community</td>
<td>Summer</td>
<td></td>
<td>20 (5–41)</td>
<td>[43]</td>
</tr>
<tr>
<td>Hungary</td>
<td>Debrecen</td>
<td></td>
<td></td>
<td>79 F</td>
<td>65</td>
<td></td>
<td>Community</td>
<td>Autumn</td>
<td></td>
<td>21 (5–54)</td>
<td>[43]</td>
</tr>
<tr>
<td>Hungary</td>
<td>Debrecen</td>
<td></td>
<td></td>
<td>60 F</td>
<td>65</td>
<td></td>
<td>Community</td>
<td>Winter</td>
<td></td>
<td>20 (5–41)</td>
<td>[43]</td>
</tr>
<tr>
<td>Poland</td>
<td></td>
<td></td>
<td>September</td>
<td>206 M</td>
<td>60 (51–81)</td>
<td>29 (17–42)</td>
<td>Healthy</td>
<td>Year</td>
<td>HPLC</td>
<td>29 (4–74)</td>
<td>[44]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td>October</td>
<td>59 M</td>
<td>60</td>
<td>28</td>
<td>Community</td>
<td>Spring</td>
<td></td>
<td>27 (4–66)</td>
<td>[44]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td></td>
<td>96 M</td>
<td>61</td>
<td>30</td>
<td>Community</td>
<td>Summer</td>
<td>HPLC</td>
<td>33 (7–74)</td>
<td>[44]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td></td>
<td>24 M</td>
<td>61</td>
<td>29</td>
<td>Community</td>
<td>Autumn</td>
<td></td>
<td>25 (6–58)</td>
<td>[44]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td></td>
<td>30 M</td>
<td>59</td>
<td>29</td>
<td>Community</td>
<td>Winter</td>
<td></td>
<td>23 (5–45)</td>
<td>[44]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td></td>
<td>65 F</td>
<td>72 ± 1</td>
<td></td>
<td>Healthy</td>
<td>Winter</td>
<td>HPLC</td>
<td>13</td>
<td>[26]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td>October</td>
<td>149 F</td>
<td>65</td>
<td>29 ± 5</td>
<td>Healthy, not treated with vitamin D, cross section</td>
<td>Winter</td>
<td>CLIA, Liaison (DiaSorin) and ECLIA, Elecsys 2010 (Roche Diagnostics)</td>
<td>13 ± 7</td>
<td>[39, 40]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td>44.2° N–52.2° N</td>
<td>2010–2011</td>
<td>124 F</td>
<td>75</td>
<td>30 ± 4</td>
<td>Healthy</td>
<td>Winter</td>
<td></td>
<td>14 ± 8</td>
<td>[39, 40]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td>25–40° E</td>
<td>2010–2011</td>
<td>711 F</td>
<td>69 (60–95)</td>
<td>29 ± 5</td>
<td>Healthy</td>
<td>Annual</td>
<td>ECLIA, Cobas e411 (Roche Diagnostics)</td>
<td>13 ± 8</td>
<td>[39, 40]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td></td>
<td>86 M</td>
<td>71 (60–91)</td>
<td>28 ± 4</td>
<td>Healthy</td>
<td>Annual</td>
<td></td>
<td>16 ± 9</td>
<td>[39, 40]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td></td>
<td>120 F</td>
<td>69 ± 6</td>
<td>30 ± 6</td>
<td>Healthy</td>
<td>Winter</td>
<td></td>
<td>11 ± 6</td>
<td>[39, 40]</td>
</tr>
<tr>
<td>Ukraine</td>
<td></td>
<td></td>
<td></td>
<td>305 F</td>
<td>68 ± 6</td>
<td>28 ± 5</td>
<td>Healthy</td>
<td>Summer</td>
<td></td>
<td>15 ± 8</td>
<td>[39, 40]</td>
</tr>
</tbody>
</table>
Table 5: Serum 25(OH)D3 concentration (ng/mL) versus age range and month measured for patients at Semmelweis University, Budapest, between April 2009 and March 2010 [9].

<table>
<thead>
<tr>
<th>Month</th>
<th>0–9 years</th>
<th>10–19</th>
<th>20–29</th>
<th>30–39</th>
<th>40–49</th>
<th>50–59</th>
<th>60–69</th>
<th>70–79</th>
<th>80–89</th>
<th>SDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>March</td>
<td>25</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>22</td>
<td>22</td>
<td>23</td>
<td>23</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>May</td>
<td>31</td>
<td>23</td>
<td>25</td>
<td>24</td>
<td>23</td>
<td>24</td>
<td>24</td>
<td>21</td>
<td>21</td>
<td>21</td>
</tr>
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<td>June</td>
<td>30</td>
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<td>30</td>
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<td>28</td>
<td>26</td>
<td>29</td>
<td>28</td>
<td>21</td>
<td>56</td>
</tr>
<tr>
<td>July</td>
<td>35</td>
<td>30</td>
<td>33</td>
<td>31</td>
<td>28</td>
<td>27</td>
<td>27</td>
<td>25</td>
<td>19</td>
<td>55</td>
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<tr>
<td>August</td>
<td>42</td>
<td>37</td>
<td>35</td>
<td>35</td>
<td>36</td>
<td>29</td>
<td>33</td>
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<td>21</td>
<td>42</td>
</tr>
<tr>
<td>September</td>
<td>36</td>
<td>30</td>
<td>30</td>
<td>29</td>
<td>30</td>
<td>29</td>
<td>26</td>
<td>26</td>
<td>16</td>
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</tr>
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<td>27</td>
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<td>20</td>
<td>15</td>
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<td>21</td>
<td>21</td>
<td>21</td>
<td>19</td>
<td>23</td>
<td>20</td>
<td>15</td>
<td>1</td>
</tr>
</tbody>
</table>

and annual values were reported as 25 ng/mL in France [41]. Thus, 25(OH)D serum concentrations of Central European and Western European countries showed consistent agreement. Some information is available in the studies regarding serum 25(OH)D concentrations in men and women. A study from Great Britain involving 45-year-olds in a cohort study found that women had statistically higher concentrations than men in winter, while men had statistically higher concentrations in summer [42]. The differences might be due to men spending more time outdoors and women taking more oral vitamin D. A study from Estonia found similar but statistically nonsignificant results: in summer, men had a mean serum 25(OH)D concentration of 24.2 ng/mL while women had 23.4 ng/mL, while in winter the values for males and females were 17.1 ng/mL and 17.8 ng/mL, respectively [32].

3.4. The Elderly. Table 4 gives serum 25(OH)D concentrations for seniors aged 60 years or older. In Central European countries, wintertime 25(OH)D concentrations ranged from 11 ng/mL in Ukraine to 20 ng/mL in Hungary. Summertime 25(OH)D concentrations ranged from 15 ng/mL in Ukraine to 33 ng/mL in Hungary. Annual 25(OH)D concentrations ranged from 13 ng/mL in Ukraine to 29 ng/mL in Hungary. In Western European countries, wintertime values ranged from 17 to 20 ng/mL. Analyzing serum 25(OH)D concentrations with respect to latitude in either Central or Western European countries revealed no consistent variability. At least in part, the reasons for this could include that the solar ultraviolet-B (UVB) dose gradient during European summer is not large above 40°N latitude and that skin pigmentation becomes lighter as latitude increases, making it easier to generate vitamin D from solar UVB [48]. As noted in Table 5, serum 25(OH)D concentrations decrease with age above about 50 years. Since most studies summarized in this table reported 25(OH)D concentrations for a limited range of ages, stated in the table, the values in the table should be considered representative of those for the age ranges studied and not for those over the age of 60 years.

3.5. Effect of Age and Season. A useful study on the variation of serum 25(OH)D3 concentration with respect to age in 10-year groupings and month of measurement (Table 5) was reported for a population from Budapest, Hungary (47°N latitude, 16.8°E longitude) [15]. Although the subjects studied were patients, nothing indicated that their morbidity affected serum 25(OH)D3 concentration. However, the report noted that, for the 1307 subjects with repeated measurements, serum 25(OH)D concentrations were lower for the second measurement (26 ± 9 ng/mL) than for the first (27 ± 13 ng/mL), suggesting that the medical staff did not recommended taking vitamin D supplements. Table 5 gives a summary of data from that study. Several months were omitted for which serum 25(OH)D3 concentrations either did not change or were inconsistent with concentrations for other months; values in January were similar to those in May. Several associations become clear from the content of Table 5: serum 25(OH)D3 concentration increased minimally before June except for the population aged 0–9 years. For all ages, serum 25(OH)D3 concentration started to decline in September and reached wintertime values by October. Peak serum 25(OH)D3 concentrations were the highest for the youngest people and the lowest for the oldest people. The wintertime mean serum 25(OH)D concentration was about 20–23 ng/mL for all ages. The increase in summer amounted to 20 ng/mL for those aged 0–9 years, 14–15 ng/mL for those aged 10–49 years, 10 ng/mL for those aged 50–69 years, and 5–6 ng/mL for those aged 70–89 years. Two primary factors accounted for age-related seasonal fluctuations (i.e., differences in summertime peak values): limited time spent outdoors in sunlight and reduced efficiency of vitamin D production from UVB irradiance. In a mid-1980s study, vitamin D production efficiency reported for people older than 60 years was about 25% of that for those younger than 20 years [49], owing to less 7-dehydrocholesterol in the skin, which is converted to vitamin D3 through the action of UVB irradiance followed by a thermal process. The change in vitamin D production in summer as a function of age agrees with the efficiency study. Those with darker skin make vitamin D more slowly than those with light skin since the melanin in the skin reduces the transmission of solar UVB to the 7-dehydrocholesterol. In addition, Table 5 gives calculated standard vitamin D doses (SDD) for whole-day irradiance for solar UVB measured in Belsk, Poland (52° N latitude, 21° E longitude) [50]. However, because vitamin D3 production is limited to 10 000–20 000 IU/day (since UV both produces...
vitamin D and destroys its metabolites), one cannot use the
SDD values to estimate vitamin D production for a given time
in the sun. For such information, the graphs in the papers
by Webb and Engelsen [51] and Bakos and Mikó [52] are
useful. Vitamin D production potential peaks near the end
of June, whereas serum 25(OH)D3 concentration peaks in
August. The lag of about 6 weeks is related primarily to the
time required to build up serum 25(OH)D concentration.
Serum 25(OH)D is the most important clinically available
measurement of vitamin D status, reflecting lifestyle and
dietary habits [53]. Determining the amount provided by
the sun or food is difficult. The duration and intensity of
exposure to sunlight are not easily measurable, and age, skin
pigmentation, sunscreens, clothing, and even window glass
reduce its effects [54]. In equatorial regions exposure to the
sun alone is adequate, but at latitudes above 40 degrees
north or south and higher, people make little vitamin D in
the winter. Measurement of serum 25(OH)D provides direct
information. Although its concentration depends on vitamin
D production and intake, its serum half-life is much longer
than that of vitamin D (weeks versus hours), and it therefore
provides an integrated assessment of vitamin D status. Serum
25(OH)D concentrations depend on age, sunlight exposure,
vitamin D dietary intake, or supplementation.

3.6. 25(OH)D Assays Used. The spectrum of methods com-
monly used in research and laboratory practice includes three
types: manual immunoassays, automated immunoassays, and
direct detection methods. Most instruments or approaches
yield reasonably accurate measurements; however, some
instruments appear problematic [44]. Several reports have
also discussed analogous pitfalls of the assays [55–59].
In a comparison of 25(OH)D assays in Sweden, a high-
pressure liquid chromatography (HPLC) assay measured 34 ±
2 ng/mL, a radioimmunoassay (RIA) measured 28 ± 2 ng/mL,
and a competitive immunochemiluminescence assay (CILA)
measured 24 ± 2 ng/mL [56]. In a comparison of assays with
liquid chromatography-tandem mass spectrometry methods
in Australia, DiaSorin Liaison, IDS, and Siemens assays met
minimum performance goals [59]. In a comparison study in
Warsaw, the Elecsys (total vitamin D) from Roche measured
about 2 ng/mL higher than the Liaison from DiaSorin
[60]. Immunoassays are sensitive to 24,25-dihydroxyvitamin
D, which can occur at concentrations up to 5 ng/mL [61].
Vitamin D-binding protein concentrations also affect the
accuracy of serum 25(OH)D concentration measurement
[62]. Some laboratories validated their assay performance
by comparing measurements with samples submitted to the
international Vitamin D External Quality Assessment
Scheme (DEQAS) [58]. Comparability of 25(OH)D results
could be facilitated if all laboratories were to participate with
DEQAS.

4. Discussion

To our knowledge, this study is the first to summarize
available data regarding vitamin D status and epidemiology in
Central European populations of different ages. Most popu-
lations and most age groups have at least a moderate deficit of
25(OH)D according to currently binding standard references.
The potential limitation we acknowledge is that all studies in
this review are either retrospective or cross-sectional. To draw
firm conclusions on intraindividual variations in 25(OH)D
levels in different seasons, a prospective study design would
be desirable. With the exception of two studies [43, 44], no
particular inclusion or exclusion criteria for study participa-
tion were assumptive; therefore, we recognize that studied
populations may have been heterogeneous. Furthermore,
25(OH)D3 and total 25(OH)D concentrations were usually
similar but not identical, so we analyzed results from studies
irrespective of type of vitamin D determination. A review
of 394 studies of unadjusted serum 25(OH)D concentrations
from around the world found a mean value of 22 ± 1 ng/mL,
with no effect of latitude for nonwhites [63]. However,
the regression fit to the data for white people went from
approximately 40 ng/mL near the equator to approximately
16 ng/mL at the poles. What happens in Europe is still
not clear from that paper. Evidently, skin pigmentation (as
well as diet at high latitudes) has adapted well to solar
UVB doses where people have lived for millennia [48].
A review of serum 25(OH)D concentrations among dark-
skinned people living in Europe—primarily those of African,
Asian, or Middle Eastern origin—supports this hypothesis.
These ethnically different groups had lower serum 25(OH)D
concentrations than the indigenous white inhabitants [64].
The three important factors contributing to the difference
were darker skin, clothing that covered more skin area, and
limited oral vitamin D intake from food. Serum 25(OH)D
concentrations in winter do not drop as low as might be
expected on the basis of solar UVB doses in winter for two
reasons: (1) the decay time of 25(OH)D is 4–6 weeks—that is,
the time it takes to drop to half its value—and (2) when serum
25(OH)D concentrations are low, the body converts vitamin
D to 25(OH)D much more efficiently [65].

The following question emerges: if the natural sources of
vitamin D that arrived at over millennia lead to mean annual
serum 25(OH)D concentrations slightly above 20 ng/mL,
why is this value not adequate? One point to be addressed
is that life expectancy has considerably increased in Europe
and elsewhere during the past century because of health
and require further long-term prospective investigation, it
is rather justified to recommend an individualized vitamin
D supplementation to all age groups in CE. The practical
approach of such a strategy is aimed to alleviate the vitamin
D status in this region—that is, to consequently diminish the
risk of 25(OH)D deficits.
5. Summary and Conclusion
The essential finding in this review is that most people living in both Central and Western Europe have serum 25(OH)D concentrations below the optimal values of 30–50 ng/mL. The main reason is that solar UVB, being the primary source of vitamin D, is limited for most CE populations; thus, producing vitamin D from solar UVB from October through March is nearly impossible above 40°N latitude. By consequence, the concentrations are particularly low from October through May, implicating the deficiency to a large extent [15]. Also, most people spend most time indoors and so they produce vitamin D only through casual sunlight exposure, which raises mean serum 25(OH)D concentration from 15 ng/mL in February to 30 ng/mL in September for individuals aged 45 years living in the UK [42]. The groups at particularly high risk of vitamin D deficiency include those largely staying indoors, pregnant and nursing women, newborns, breast-fed infants without vitamin D supplementation, overweight or obese people [72], patients with chronic or infectious disease, and those older than 50 years. A variety of preventive means and interventions can be implemented in CE to increase serum 25(OH)D concentrations, including increased but reasonable solar UVB irradiance, fortification of food, and augmented consumption of vitamin D supplements.

Conflict of Interests
William B. Grant receives funding from Bio-Tech Pharmacal (Fayetteville, AR) and the Sunlight Research Forum (Veldhoven) and has received funding from the UV Foundation (McLean, VA), the Vitamin D Council (San Luis Obispo, CA), and the Vitamin D Society (Canada). Other authors declare that there is no conflict of interests regarding the publication of this paper.

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