Relationship between vitamin D and red blood cell indices in South Asians and White Europeans

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Vitamin D has been implicated in a broad range of physiological systems including bone and mineral metabolism, cellular proliferation and differentiation, and erythropoiesis.[1–3] These and other findings lead to the proposition that population supplementation with vitamin D will be beneficial.[4–6] Sim and colleagues have suggested that vitamin D has a role in erythropoiesis, and that deficiency brings a risk of anaemia, with lower haemoglobin and higher usage of erythrocyte-stimulating agents.[5]

It has long been recognised that South Asian ethnicity is associated with low levels of vitamin D.[7,8] This same population is also at risk of low haemoglobin and anaemia, potentially as a consequence of haemoglobinopathy.[9] The work of Sim *et al.*,[5] in a population of subjects free of chronic kidney disease, reported vitamin D levels in black versus non-black subjects. Although they found that racial background failed to be associated with vitamin D, this prompted the authors of the present study to test the hypothesis that there is a relationship between vitamin D status, red blood cell indices and South Asian ethnicity. To control the study, the authors compare South Asians and White Europeans with respect to vitamin D data, and related routine biochemistry indices, and white cell and platelet counts.

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Data were harvested from the hospital pathology laboratory computer, where vitamin D was assessed by a single method, and where age was >16 years. The authors collected age (years), gender (male/female) and ethnicity (self-reported South Asian or White European, mixed race excluded). South Asian ethnicity includes those from India, Pakistan, Bangladesh and Sri Lanka. Routine biochemistry indices were vitamin D (as 25-hydroxycholecalciferol, liquid chromatography mass spectrometry after extraction in *n*-hexane), parathyroid hormone (PTH; immunoassay), calcium (colorimetric), albumin (bromocresol green) and alkaline phosphatase (colorimetric). Haematology indices (white cell count [WCC], haemoglobin, mean cell volume [MCV], mean cell haemoglobin [MCH] and platelets) were measured on an autoanalyser.

Data were collected from 2185 South Asians (mean age: 42 years [SD: 16]), of whom 1551 were women (72%), and from 827 White Europeans (mean age: 54 years [SD: 19]), of whom 559 were women (67%). The higher proportion of South Asians, their younger age and greater proportion of women presumably reflects bias in requesting vitamin D measurement, perhaps for osteomalacia, and is itself notable. In order to match for age and gender, South Asians were randomly deleted until, as a group, their age and gender ratio was comparable to that of the White Europeans (Table 1).

Sets of data were analysed by χ^2 testing for categorical indices, *t*-test for continuous indices with a normal distribution. and the Mann-Whitney U test for continuous indices with a non-normal distribution. Data were correlated by Spearman's method, and a binary logistic regression

Table 1. Demographic and biochemistry indices.

		South Asians	White Europeans	*P* value
Age (years)	All (*n*=1182/808)	53.8 (12.4)	54.4 (19.4)	0.379
	Men (*n*=368/260)	54.8 (13.1)	56.9 (19.2)	0.120
	Women (*n*= 813/548)	53.3 (12.0)	53.2 (19.4)	0.896
Vitamin D (nmol/L)	All	21.7 (14.2–35.7)	30.8 (20.7–48.6)	<0.001
	Men	21.6 (14.3–33.8)	31.0 (19.4–46.6)	<0.001
	Women	21.8 (14.2–36.7)	30.7 (21.4–49.0)	<0.001
PTH (pg/mL)	All	52.5 (39.2–71.2)	49.0 (36.0–66.5)	0.360
	Men	52.0 (36.7–66.0)	50.0 (35.7–65.0)	0.701
	Women	50.5 (40.2–88.5)	48.0 (36.0–71.7)	0.344
Calcium (mmol/L)	All	2.25 (0.10)	2.27 (0.12)	<0.001
	Men	2.25 (0.11)	2.27 (0.12)	0.019
	Women	2.24 (0.10)	2.26 (0.11)	<0.001
Albumin (g/L)	All	45.0 (2.7)	45.2 (3.1)	0.072
	Men	45.9 (2.5)	45.8 (3.3)	0.679
	Women	44.6 (2.6)	45.0 (2.9)	0.015
Alkaline phosphatase (IU/L)	All	79.2 (28.8)	77.8 (35.2)	0.334
	Men	80.1 (30.5)	78.3 (37.0)	0.521
	Women	78.8 (27.0)	77.5 (34.3)	0.462

Data analysed by χ^2, *t*-test or the Mann-Whitney U test. Data presented as mean (SD) or median (inter-quartile range).
PTH: Parathyroid hormone.

Table 2. Haematology indices.

		South Asians	White Europeans	*P* value
WCC (x10⁹/L)	All	6.9 (1.8)	6.6 (1.9)	<0.001
	Men	7.1 (1.9)	6.6 (1.0)	<0.001
	Women	6.8 (1.8)	6.5 (1.9)	0.022
Haemoglobin (g/L)	All	129 (17)	132 (1.6)	<0.001
	Men	143 (15)	141 (16)	0.238
	Women	123 (14)	127 (14)	<0.001
MCV (fL)	All	85.4 (7.3)	89.6 (7.2)	<0.001
	Men	87.1 (6.3)	90.2 (6.5)	<0.001
	Women	84.7 (7.6)	89.3 (7.4)	<0.001
MCH (pg)	All	27.5 (2.9)	29.1 (2.8)	<0.001
	Men	28.6 (2.4)	29.7 (2.7)	<0.001
	Women	27.0 (3.0)	28.8 (2.8)	<0.001
Platelets (x10⁹/L)	All	272 (71)	260 (73)	<0.001
	Men	242 (62)	237 (76)	0.375
	Women	285 (70)	271 (68)	<0.001

Data analysed by *t*-test.

model was used to determine those indices that were linked to ethnicity. Data were analysed without regard to gender, and again separately.

Table 1 shows age and biochemistry data from the 1900 subjects. South Asians, irrespective of gender, had lower vitamin D levels, and South Asian women had lower calcium and albumin levels than did White European women.

Table 2 shows the haematology indices. The WCC was higher in South Asians, irrespective of gender, but haemoglobin was lower only in South Asian women. Furthermore, MCV and MCH were lower in South Asians, irrespective of gender, while South Asian women had a higher platelet count.

In an analysis of all subjects, vitamin D correlated inversely with PTH (r=–0.28) and positively with MCV (r=0.19) and age (r=0.19) (all P<0.001). In the regression model, only vitamin D and WCC (both P<0.001) were linked to ethnicity. In an analysis of the 628 men, vitamin D correlated inversely with PTH (r=–0.3) but positively with calcium (r=0.16) (both P<0.001). The regression analysis linked vitamin D, WCC and MCV to ethnicity (all P<0.001). In an analysis of the 1362 women, vitamin D correlated inversely with PTH (r=–0.26) and positively with MCH (r=0.23), MCV (r=0.22), calcium (r=0.18) and haemoglobin (r=0.15) (all P<0.001). In the regression analysis, only vitamin D (P<0.001) and WCC (P=0.038) were linked to ethnicity.

In each of the four groups, vitamin D increased modestly with age (South Asian women: r=0.19, South Asian men: r=0.15, White European women: r=0.22, White European men: r=0.19) (all P<0.005). However, MCH increased with age in the women (South Asian: r=0.16, White Europeans: r=0.21) (both P<0.001) but not the men (r=–0.005 [P=0.923] and r=0.061 [P=0.325] in South Asians and White Europeans, respectively). Conversely, haemoglobin fell markedly with age in both groups of men (r=–0.365 in South Asians, r=–0.43 in White Europeans [both P<0.001]) but not in the women (r=0.049 [P=0.167] in South Asians, and r= –0.038 [P=0.375] in White Europeans).

This study has confirmed lower levels of total vitamin D in South Asians compared to White Europeans.[7,8] However, the scale of this reduction, to approximately 70%, is considerably less than that reported in another UK study, where levels in South Asians were only 30% of the levels of the local white control group.[10] The reasons for this are unclear but may reflect recruitment bias. Levels of vitamin D were no different between the men and women studied. Unlike others workers,[7,8,10] all of whom reported raised PTH in Asian Indians (potentially reflecting the low vitamin D), the present study found no difference in PTH between the ethnic groups. The strong correlation between PTH and vitamin D in all four groups is likely to reflect the established common metabolic pathway.

The likely reasons for the markedly lower levels of vitamin D found in South Asians is that the relatively low sunlight exposure in the UK fails to promote the synthesis of vitamin D.[8] Indeed, increasing exposure to sunlight increases serum vitamin D,[11] and lighter skin absorbs more ultraviolet light, leading to higher vitamin D,[12] and a call to revise the recommended sunlight exposure for South Asians.[13] Although the present study found some marginally statistically significant differences in certain indices, in many cases these can be accounted for by the high degree of power. For example, the lower albumin levels in South Asian women (P=0.015) is probably irrelevant in a clinical setting, the difference being less than 0.9%. Similarly, South Asian women were found to have lower calcium levels than White European women (0.9%), but this may be a spurious finding as Ward *et al.*, in a better controlled study, failed to find a difference.[10]

The data compared in the present study came from general practitioner requests to the hospital for vitamin D levels, presumably to investigate a potential pathology or a suspected low level. Therefore, it is likely that a significant proportion of this population will be carrying one or more potential pathologies (e.g., haemoglobinopathy) known to be present in South Asians[9] and presumed to be absent in

White Europeans. This may account for the lower red cell indices in the South Asians, and possibly the higher platelet and white cell counts. Notably, the study of Sim *et al*.[5] excludes those with haemoglobinopathy and other causes of anaemia. Although PTH did not differ between the ethnicities, it correlated inversely with vitamin D in all groups, reflecting physiology.

An additional caveat is that no data were available on the ingestion of vitamin D supplements. However, the authors would be surprised if the 30% relative increase in level seen in White Europeans was due to ingestion of supplements rather than their lighter skin. Nevertheless, irrespective of the aetiology of the low vitamin D in South Asians, the data studied here indicate that there is no evidence that this deficiency has major implications for red blood cell biology. □

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