Original Article

Vitamin D status and cardiometabolic risk factors in young adults in Hong Kong: associations and implications

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Background and Objectives: Vitamin D deficiency is reportedly common, but we lack data from young adults. Such data are of interest because epidemiological data support vitamin D as a possible risk modulator for diabetes and cardiovascular ('cardiometabolic') disease. Our objectives were to assess vitamin D status (as plasma 25(OH)D concentration) and investigate associations between this and biomarkers of cardiometabolic disease risk in a group of still-healthy young adults in Hong Kong. **Methods and Study Design:** In this observational study, fasting venous blood was collected from 196 (63 males, 133 females), young (18-26 years) non-smoking, non-obese, consenting adults in good general health. Plasma 25(OH)D was measured by LC-MS/MS. A panel of established cardiometabolic risk factors (HbA1c, plasma glucose, lipid profile, hsCRP) and blood pressure were also measured. **Results:** Mean (SD) plasma 25(OH)D concentration was 42.1 (13.0), with range 15.7-86.8 nmol/L; 141/196 subjects (72%) had vitamin D deficiency (25(OH)D <50 nmol/L); 13/184 (6.6%) were severely deficient (<25 nmol/L). Inverse association was seen between 25(OH)D and fasting glucose (r=-0.18; p<0.05). Higher HbA1c and TC:HDL-C ratio and lower HDL-C were seen in those with plasma 25(OH)D <25 nmol/L (p<0.05). **Conclusions:** Vitamin D deficiency was highly prevalent and associated with poorer cardiometabolic risk profile in these young adults. Public health strategies for addressing vitamin D deficiency are needed urgently. These new data provide support for further study on vitamin D deficiency as a modifiable risk factor for cardiometabolic disease and the ameliorative effects of increased vitamin D intake on cardiometabolic disease risk profile of vitamin D-deficient young adults.

Key Words: vitamin D, 25(OH)D, cardiometabolic disease, diabetes, public health

INTRODUCTION

There is evidence that vitamin D deficiency increases risk of non-communicable diseases (NCDs), including diabetes and cardiovascular disease (CVD).[1-4] The currently accepted way to assess vitamin D status is by measurement of plasma 25(OH)D (calcidiol) concentration.[1-4] Plasma 25(OH)D <30 nmol/L is linked strongly to mortality from cancer, cardiovascular and respiratory diseases, as well as death from all-causes, and risk increases at <75 nmol/L.[4] Plasma 25(OH)D <50 nmol/L is generally agreed as deficient, and though levels ≥50 nmol/L may suffice for bone health, this is disputed, and 25(OH)D of 75-100 nmol/L has been recommended for maintenance of health in non-skeletal systems, and for bone health, especially in the elderly.[5-8]

Vitamin D is found in some natural and fortified foods, and supplements are available. There are two forms of pre-vitamin D, D2 from fungal sources (e.g. field grown mushrooms), and D3, of animal origin.[1,2,7,9] Various reports on recommended and upper tolerable dietary intakes of vitamin D are available.[5-7,9] However, a major source of vitamin D (as D3) is cutaneous synthesis in sun-exposed skin, and in most healthy people 10-15 min/day of direct exposure of skin to sunshine is sufficient to prevent deficiency.[1,2,10,11] Nonetheless, vitamin D deficiency is common. A systematic review involving >168,000 subjects from 44 countries showed that 88% of subjects had plasma/serum 25(OH)D <75 nmol/L, and in 37% it was

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<50 nmol/L.[12] In the HELENA study of 1,006 adolescents (12-17 years) from nine European countries, 81% had 25(OH)D <75 nmol/L, 42% had levels <50 nmol/L and 15% were severely deficient (defined in that study as <27.5 nmol/L).[13] Vitamin D deficiency is common even in sunny countries. In Singapore, 42% of 114 men and women (21-100 years) had 25(OH)D <50 nmol/L, in Qatar, 62% of children (11-16 years) had 25(OH)D <50 nmol/L, and in Iran 96% of 216 girls (14-17 years) had 25(OH)D <50 nmol/L, and a very low mean (SD) value of 18.1 (7.0) nmol/L was found.[14-16] The high prevalence of vitamin D deficiency is alarming, given its association with increased NCD and mortality risk in addition to its clear links to skeletal problems.[1-4,7,8] In particular, deficiency of vitamin D from a young age could have profound effects on health in later life, making it a serious public health problem.

Hong Kong is an affluent, modern city located at latitude 22° North, with abundant sunshine most of the year. Still, 18% and 92%, respectively, of 221 premenopausal women studied had 25(OH)D ≤25 and ≤50 nmol/L.[17] As in other areas of the world, the main causes of vitamin D deficiency are deficient dietary intake and the modern, largely indoor lifestyle that, coupled with the well publicised links between sunshine and skin ageing and skin cancer, as well as certain cultural factors, leads to inadequate cutaneous exposure to sunshine.[1,2,15-17] Vitamin D status is improved by higher exposure to sun, taking food naturally rich in or fortified with vitamin D or by use of supplements.[1,2,6-11] However, currently we lack local data on vitamin D status of young adults and so do not know the scale of the problem in our young people, or its potential biological impact on NCD risk. Such data are needed to help guide public health policy in regard to, for example, promotion of dietary and other strategies to prevent deficiency, and screening programmes for identifying vitamin D deficient individuals for targeted intervention. CVD is the leading cause of death worldwide, there is a global pandemic of type 2 diabetes, CVD risk is markedly increased in diabetes, and in Hong Kong the all-age prevalence of type 2 diabetes is high (~10%).[18] Diabetes and CVD are associated with subtle but progressive underlying biochemical and cellular changes that take many years to develop into overt disease.[19] Determining and addressing NCD risk factors in early adult life is a cost-effective means to promote healthy ageing. 'Primordial' and primary prevention strategies are needed, and are relevant especially to CVD and type 2 diabetes ('cardiometabolic disease'), and to Asia, where the rate of cardiometabolic disease is fast increasing alongside rapid lifestyle changes.[19-21] Importantly then, if vitamin D deficiency is confirmed as a new risk factor for cardiometabolic disease, there are significant implications for the long-term health of young vitamin D deficient adults regardless of where they live. The aims of this study were to determine vitamin D status in a group of young, still healthy adults in Hong Kong, and to investigate associations between this and biomarkers of cardiometabolic disease risk.

METHODS

Study population

196 volunteers (63 males, 133 females) were recruited by poster, email and word of mouth. They were mainly university or higher education college students and all had been living in Hong Kong for at least 1 year. All but two of the volunteers were of Chinese ethnicity. Inclusion criteria were: age 18-26 years, non-smoker, not obese, in self-reported good general health, not taking regular medication or any vitamin or food supplements, no hospitalization in the previous year, no medical treatment in the previous six months. This information was collected during a face-to-face interview, before sample collection, during which a checklist was completed by a member of the research team and each volunteer answered a set of questions on the inclusion and exclusion criteria. Body mass index (BMI) was calculated by dividing the body weight (in kg) by the square of height (in m). These measurements were performed within the same week as blood sampling. For obesity thresholds, WHO states that having a BMI of ≥30 kg/m^2 is obese; for Chinese adults living in Hong Kong, the Hong Kong Centre for Health Protection classifies BMI of ≥25.0 kg/m^2 as obese.[22,23] These were the guidelines we followed for our non-Chinese and Chinese volunteers, respectively.

Ethical approval

Ethical approval for the study was obtained from The Hong Kong Polytechnic University Human Subjects Ethics Review Committee. All procedures involving human subjects complied with the Declaration of Helsinki. All subjects gave their written informed consent. Fasting venous blood was collected, between 9.00-10.00am, on one occasion only from each volunteer, but throughout the year (n=29 in September to November, n=61 in December to February; n=98 in March to May and n=8 in June to August). Blood was placed into EDTA (for HbA1c), sodium fluoride (for glucose) and heparinized blood collection tubes. EDTA whole blood samples were stored at 4°C and HbA1c was measured within 5 days of collection. Fluoride oxalate and heparinized plasma was separated within 1h of collection. Plasma glucose was measured within 2h, and for the other biomarkers heparinized plasma was aliquoted and stored at -80°C until thawed, once only, for measurement. Plasma 25(OH)D measurement was by gradient liquid chromatography with tandem mass spectrometry (LC-MS/MS).[24] HbA1c and plasma glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (Tg) and high sensitivity C-reactive protein (hsCRP) were measured by commercially available methods. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation,[25] and the TC:HDL-C ratio, a good predictor of CVD risk irrespective of other factors, was calculated.[26] In addition, Log(Tg:HDL-C), an atherogenic index which reportedly correlates with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma, was calculated.[27] Blood pressure (average of three readings taken within a 5 min period) was measured by automated sphygmanometer.

Statistical analysis

For data handling and statistical analysis, Graphpad Prism 5 (San Diego, CA, USA) and SPSS version 21 (Armond, NY, USA) were used. In this study, we regarded plasma 25(OH)D <50 nmol/L as deficient following Institute of Medicine and Endocrine Society guidelines, and we further categorized <25 nmol/L as severely deficient, 50-74 nmol/L as inadequate, and ≥75 nmol/L as sufficient, following guidelines of the Endocrine Society.[5-8,28] Association between 25(OH)D and cardiometabolic risk factors was investigated using Pearson's or Spearman's correlational analysis, as appropriate for distribution, and biomarker differences across 25(OH)D status categories were investigated using ANOVA with Newman-Keuls post-test. Gender difference in 25(OH)D and cardiometabolic biomarkers was explored using the unpaired t-test or the Mann-Whitney test, as appropriate for distribution of data. To further investigate inter-relationships between vitamin D status while controlling for different cardiometabolic risk factors, MANOVA was performed, and MANCOVA was used to adjust for gender as a covariant. Relative numbers of males and females in each category of vitamin D status were compared using the chi-square test. Possible differences in frequencies of elevated cardiometabolic risk factors across the categories of vitamin D status were investigated by the chi-square for trend test. A p value <0.05 was regarded as statistically significant.

RESULTS

Subject characteristics are shown in Table 1. Plasma 25(OH)D and cardiometabolic biomarkers results, overall and by gender, are presented in Table 2. All vitamin D detected in subjects' plasma was D3, and no significant differences were seen in plasma 25(OH)D in relation to time of year when blood was collected (data not shown). Plasma 25(OH)D values overall ranged from 15.7 to 86.8 nmol/L. Only two subjects (both male) had 25(OH)D ≥75 nmol/L. Results showed that 141/196 (72%) of the young adults studied were deficient in vitamin D, with 13 of these subjects (~7%) severely deficient (25(OH)D <25 nmol/L).

Plasma 25(OH)D was inversely associated with fasting plasma glucose: r=-0.18; p<0.05. As shown in Table 3, slightly but significantly higher (p<0.05) HbA1c and TC:HDL-C ratio and lower (p<0.05) HDL-C were seen in those with plasma 25(OH)D <25 nmol/L. Log(Tg:HDL-C) was higher (p=0.051) in the lowest vitamin D category, and when multivariate analysis was performed controlling for the effect of other biomarkers, the difference in Log(Tg:HDL-C) in this category became statistically significant (p=0.04). No changes were seen in significance level for any of the other biomarkers after multivariate analysis. No significant difference or association was seen in relation to 25(OH)D and hsCRP or blood pressure. In terms of gender differences, the young men had significantly higher 25(OH)D (by ~12%; p<0.05) (Table 2). Still, 60% of the young men had 25(OH)D <50 nmol/L. For the cardiometabolic risk factors, and as shown in Table 2, young men had slightly but statistically significantly higher (p<0.05) blood pressure and TC:HDL-C ratio and lower HDL-C. There was no significant difference (p>0.05) in the relative numbers of males and females in each category of vitamin D status. Furthermore, adjusting for gender using MANCOVA did not change the findings of the biomarker differences across the vitamin D categories. Table 4 shows the frequencies of subjects in each category of vitamin D status who were revealed to have a

Table 1. Characteristics of the 196 subjects studied

	Total (n=196)	Males (n=63)	Females (n=133)
Age (y)	20.8 (1.6)	20.9 (1.9)	20.7 (1.5)
Height (cm)	163 (8.8)	171 (8.3)	160 (6.1)
Weight (kg)	56.7 (9.5)	62.5 (9.7)	53.9 (8.1)
BMI(kg/m^2)	21.1 (2.4)	21.2 (2.2)	21.1 (2.5)

†Data expressed as mean
‡All but two of the volunteers were of Chinese ethnicity

Table 2. Cardiometabolic risk biomarker results in the 196 young (18-26 years) apparently healthy adults studied

	All subjects	Males	Females
25(OH)D (nmol/L)	42.1 (13.0)	45.3 (14.4)	40.6 (12.1)*
BMI (kg/m^2)	21.1 (2.4)	21.2(2.2)	21.1(2.5)
SBP (mmHg)	113 (10.0)	119 (10.0)	110 (8.6)*
DBP (mmHg)	64.1 (7.7)	66.1 (8.2)	63.0 (7.3)*
FPG (mmol/L)	5.22 (0.45)	5.29 (0.58)	5.18 (0.36)
HbA1c (%)	5.29 (0.51)	5.31 (0.54)	5.29 (0.49)
TC (mmol/L)	4.60 (0.78)	4.61 (0.89)	4.59 (0.72)
HDL-C (mmol/L)	1.51 (0.30)	1.43 (0.28)	1.54 (0.31)*
LDL-C (mmol/L)	2.72 (0.63)	2.79 (0.72)	2.69 (0.59)
TC:HDL-C ratio	3.12 (0.58)	3.29 (0.68)	3.03 (0.50)*
Tg (mmol/L)	0.80 (0.33)	0.87 (0.36)	0.79 (0.31)
Log(Tg:HDL-C)	-0.28 (0.19)	-0.31 (0.19)	-0.23 (0.19)
hsCRP (mg/L)	0.50 (0.84)	0.66 (1.08)	0.42 (0.70)

†Data expressed as mean
*p<0.05 compared to value in males

Table 3. Biomarker results [mean (SD)] in different categories of vitamin D status

	25(OH)D (nmol/L)			$p^{\dagger}$	$p^{\ddagger}$	$p^{\S}$
	<25	≥25<50	≥50			
n	13	128	55			
Females/males	11/2	90/38	32/23	0.112¶	-	-
25(OH)D (nmol/L)	*20.2 (2.72)	37.2 (6.53)	58.8 (7.34)	<0.01	-	-
Body mass index (BMI) (kg/m^2)	21.9 (3.72)	21.1 (2.26)	21.0 (2.21)	0.440	0.408	0.380
Systolic blood pressure (SBP) (mmHg)	114 (13.2)	112 (10.1)	114 (9.14)	0.253	0.349	0.361
Diastolic blood pressure (DBP) (mmHg)	61.9 (7.54)	63.7 (7.97)	65.2 (7.09)	0.271	0.322	0.466
FPG (mmol/L)	5.26 (0.42)	5.25 (0.46)	5.12 (0.41)	0.166	0.141	0.093
HbA1c (%)	*5.69 (0.52)	5.25 (0.50)	5.30 (0.49)	0.013	0.013	0.013
TC (mmol/L)	4.45 (0.82)	4.54 (0.70)	4.76 (0.91)	0.17	0.246	0.235
HDL-C (mmol/L)	*1.30 (0.23)	1.53 (0.31)	1.50 (0.29)	0.027	0.028	0.015
LDL-C (mmol/L)	2.72 (0.68)	2.65 (0.56)	2.87 (0.75)	0.093	0.147	0.163
TC/HDL-C ratio	*3.50 (0.79)	3.03 (0.52)	3.23 (0.59)	0.005	0.007	0.005
Tg (mmol/L)	0.95 (0.46)	0.78 (0.29)	0.86 (0.36)	0.195	0.137	0.125
Log(Tg:HDL-C)	-0.17 (0.22)	-0.31 (0.19)	-0.26 (0.19)	0.051	0.036	0.024
hsCRP (mg/L)	0.37 (0.50)	0.52 (0.86)	0.47 (0.88)	0.871	0.794	0.786

*$p<0.05$ compared to the values in the other two categories of vitamin D status. † p value for ANOVA; $^{\ddagger}p$ value for MANOVA; $^{\S}p$ value for MANOVA adjusted with gender; ¶ p value for chi-square test.

Table 4. Frequency of each cardiometabolic risk factor [n (%)] in the elevated risk range according vitamin D status

	25(OH)D (nmol/L)			Elevated risk for biomarker defined as [source]
	<25	≥25<50	≥50	
n	13	128	55	
SBP	2 (15.4)	6 (4.7)	2 (3.6)	≥130 mmHg [30]
DBP	0 (0)	0 (0)	0 (0)	≥85 mmHg [30]
FPG	4 (30.8)	21 (16.4)	6 (10.9)	≥5.6 mmol/L [29]
HbA1c	7 (53.8)	31 (24.2)	12 (21.8)	≥5.7% [29]
TC	3 (23.1)	32 (25.0)	21 (38.2)	>5.0 mmol/L [30]
HDL-C	2 (15.4)	11 (8.6)	4 (7.3)	<1.0 mmol/L for men <1.2 mmol/L for women [30]
LDL-C	4 (30.8)	34 (26.6)	24 (43.6)	>3.0 mmol/L [30]
TC:HDL-C ratio	2 (15.4)	6 (4.7)	5 (9.1)	>4.0 [30]
Tg	2 (15.4)	2 (1.6)	1 (1.8)	>1.7 mmol/L [30]
Log(Tg:HDL-C)	2 (15.4)	2 (1.6)	3 (5.5)	>0.11 [27]
hsCRP	0 (0)	4 (3.1)	1 (1.8)	>3.0 mg/L [31]

biomarker in the elevated risk range. The threshold used for elevated risk for each biomarker is also given.[27,29-31] The % of subjects with elevated FPG or HbA1c in the <25 nmol/L category was greater than in the other two categories, but this did not reach statistical significance. Overall, >70% of subjects had one or more cardiometabolic biomarkers in the elevated risk category.

DISCUSSION

"Today's risk factors become tomorrow's cardiovascular events".[20] However, and importantly, early intervention targeted towards modifiable risk factors can prevent or delay CVD and other NCDs, including type 2 diabetes.[32] The underlying changes that lead to cardiometabolic disease begin years before overt disease develops, and include initially small changes in biomarkers of inflammation, glycaemic index, lipid metabolism and blood pressure.[19-21,24,26,32] This makes young adults a key target subgroup for preventive healthcare strategies. However, cardiometabolic biomarkers are not often monitored in healthy young adults, and remain 'hidden' until the pathological effects of advanced changes become apparent in later life. The burden of cardiometabolic diseases is such that early interventions that lower risk, even slightly, would have large socioeconomic impact.[32] From this study and other studies, deficiency of vitamin D is clearly highly prevalent even in affluent areas where there is no lack of available sunshine or food. It is noted that poor vitamin D status could be a simple bystander or a consequence rather than a cause of disease, especially in older people, and it is lower in obese subjects, especially in association with abdominal obesity.[33] However, the vitamin D receptor is present in most cell types, pleiotropic effects of vitamin D, including on the cardiovascular system and insulin secretion and action, have been demonstrated in cell culture and animal studies, and low 25(OH)D associates strongly with higher risk of cardiometabolic disease and mortality.[1,3,4,7,8,34] These findings combine to make a compelling case for the study of vitamin D as a modulator of cardiometabolic disease risk.

The role of vitamin D as a modifiable risk factor for cardiometabolic disease remains to be confirmed, and currently there is no clear consensus on what constitutes 'optimal' plasma 25(OH)D. The US Institute of Medicine

recommends ≥50 nmol/L to ensure bone health, but this is keenly debated.[5,6] A recent report recommended 50-75 nmol/L for those aged 05-64 years, but this is a wide range, and the recommendation was an "assumption" based on bone mineral density and potential protective effects against colorectal cancer.[7] The same report recommended 75-100 nmol/L for those ≥65 years, based on fracture risk in the elderly. Similarly high levels of 25(OH)D have been proposed for prevention of various disorders, including cancer, CVD, respiratory infections, diabetes and depression.[4,6,8,28] It is noted that there are some reports of adverse effects of very high levels of 25(OH)D (>100 nmol/L), however such high levels are seen only with unnecessary or excessive supplementation.[1,2,7-9]

In this study, 194/196 of the young adults studied had 25(OH)D <75 nmol/L, 72% had levels <50 nmol/L, and ~7% had plasma 25(OH)D <25 nmol/L. These figures are alarming given the strong association reported between poor vitamin D status and NCD risk.[3,4,8,34] Furthermore, we saw evidence of small but potentially important changes in cardiometabolic profile in association with vitamin D deficiency in these still-healthy young subjects, regardless of gender. Higher HbA1c and TC:HDL-C and lower HDL-C were seen in subjects who had 25(OH)D <25 nmol/L, and there was evidence also of higher Log(Tg:HDL-C) in these subjects. Furthermore, a weak though statistically significant inverse correlation between 25(OH)D and fasting plasma glucose was seen. Increased fasting glucose has clear links to risk of type 2 diabetes, lower HDL-C, elevated TC/HDL-C ratio and Log (Tg:HDL-C) increase CVD risk, and Type 2 diabetes markedly increases CVD risk.[19,26,27,32]

The high prevalence of vitamin D deficiency in young adults and its links, even if weak, to a poorer cardiometabolic risk profile have important implications for planning and implementation of public health strategies to address this 'epidemic' of what is an easily correctable deficiency, and for promotion of healthy aging through nutritional and lifestyle choices. The new data presented here provide support for vitamin D as a possible risk factor for cardiometabolic disease, especially in young, still-healthy men and women. This group is rarely studied but is a key target group for preventive health care. In previous studies of vitamin D status and cardiometabolic disease risk factors, some significant associations have been reported, though data on healthy young adults are scarce. A study with 1,739 middle-aged Framingham Offspring Study participants who were free of CVD at entry found that those with 25(OH)D concentration <37.5 nmol/L had significantly higher systolic BP, TC:HDL-C ratio and higher diabetes rates compared with those with baseline 25(OH)D concentration ≥37.5 nmol/L.[35] During a mean 5.4 years of follow-up, there were 120 cases of incident CVD, and a 62% higher risk of developing CVD was found in those with baseline 25(OH)D <37.5 nmol/L (95% CIs 1.11, 2.36, $p<0.05$).[35] More recently, a Slovakian study of 411 non-diabetic subjects found that ~50% were deficient in vitamin D (25(OH)D <50 nmol/L), and those with low vitamin D status had higher numbers of cardiometabolic risk factors, though no association between lipids and vitamin D was seen.[36] However, the subjects' age range was wide (18-81 years), and included smokers, hypertensive and obese subjects, factors that could have confounded results. A smaller study from Singapore presented data from 114 healthy subjects (59 men, 55 women) covering a very wide age range (21-100 years) and reported that 42% were deficient in vitamin D (25(OH)D <50 nmol/L), and that 25(OH)D was inversely associated with TC:HDL-C ratio and insulin resistance.[14] In contrast, a study of 235 South Asians (20-79 years) living in Canada showed no association between vitamin D and predictive cardiometabolic risk factors.[37] None of these previous studies showed separate data on young adults. In the HELENA study of European adolescents (12-17 years), lower vitamin D status increased ($p<0.05$) the odds of higher insulin resistance, but only in females,[38] and a Danish study of 782 children (8-11 years) showed that vitamin D status correlated inversely with plasma lipids and metabolic syndrome index, and that a 10 nmol/L increase in 25(OH)D associated significantly ($p<0.05$) with lower diastolic blood pressure, TC, LDL-C and triglycerides, although the effect sizes were small.[39] It is noted that in this current study of 18-26 year olds, the associations between low vitamin D status and poorer glycaemic control and lipid parameters, while significant, were modest. Still, even modest improvement to cardio-metabolic profile could have significant positive impact on future health and bring socioeconomic benefits. Therefore, the findings presented here are of interest, add to current evidence of vitamin D deficiency in relation to risk of cardiometabolic disease, and extend previous findings by furnishing data on young, non-obese and still healthy adults.

There have been many vitamin D supplementation studies, though as yet evidence of benefit is unclear. A Cochrane Review concluded that "long-term supplementation of vitamin D may have a beneficial effect on overall mortality, especially in patients with vitamin D insufficiency and younger than 80 years".[40] It is outside the scope of this paper to review supplementation studies, but a few points are worth highlighting. Supplementation studies have generally been of fairly short duration (3-4 months) and have involved older adults and those already suffering from or at high risk of disease. Doses have varied greatly (from a few hundred units vitamin D added to daily intake, to injection of 300,000 units or more). Some studies have supplemented non-deficient subjects, or did not monitor plasma 25(OH)D response. Also, it may be that vitamin D supplementation was simply given too late in life and for too brief a time to make a significant impact on health outcomes or established disease. To isolate the potentially ameliorative effect of correction of deficiency, low vitamin D status has to be an inclusion criterion, and plasma 25(OH)D (and perhaps other vitamin D metabolites) response to supplementation must be monitored. Furthermore, studying subtle cardiometabolic effects of correction of vitamin D deficiency in young adults may offer a more rewarding approach than seeking short-term effects in older adults at high risk of or with established disease.

The strengths of this current study are its focus on healthy subjects in early adulthood, the specific and sensitive method used for plasma 25(OH)D, and the fairly

comprehensive panel of cardiometabolic biomarkers measured. Low vitamin D status may be a consequence of advanced age, obesity, and pre-existing advanced disease.[1,2,33,34] Focusing on non-obese, non-smoking and still-healthy young adults avoids these confounders. Still, this study has several limitations, and we do not wish to overstate our findings. This was an observational study, and our group of 196 young people is small in comparison to some other studies, and cannot to be said to be completely representative of young adults in Hong Kong. Subjects were mainly university students and there were more females than males. This could have introduced some bias. Still, there is no reason to believe that the overall lifestyle of our subjects is much different from their peers in this modern metropolis, or indeed in other modern cities, and our group was quite homogenous: subjects were within a narrow age range, non-smoking, non-obese, in self-reported good general health, and living within a small geographical area. However, given our group's characteristics, the high numbers of subjects with one or more cardiometabolic disease biomarker in the elevated risk range was unexpected and this finding is worthy of further study, regardless of the role of vitamin D.

In conclusion, the data presented here add to a growing database of vitamin D status from various parts of the world, and reveal very high prevalence of deficiency in a group of young healthy adults, a previously understudied group. Results also show interesting, albeit modest, associations between vitamin D deficiency and poorer cardiometabolic risk profile in this group. Long-term deleterious effects of vitamin D deficiency from early adult life may be profound, given the strong associations reported between deficiency and risk of CVD and type 2 diabetes, and considering also the huge burden of such diseases worldwide, which is increasing fastest in the Asia-Pacific region. These new data provide support for further investigations into vitamin D deficiency as a possible and, importantly, a modifiable risk factor for cardiometabolic disease, and highlight the urgent need for public health strategies to address the 'epidemic' of vitamin D deficiency, especially in our young people.

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AUTHOR DISCLOSURES

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