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Vitamin D and parathyroid hormone status in a representative population living in Macau, China

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ABSTRACT

Associations between documented sun-exposure, exercise patterns and fish and supplement intake and 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) were investigated in a random household survey of Macau residents (aged 18–93). Blood samples (566) taken in summer were analyzed for 25OHD and PTH.

In this Chinese population, 55% were deficient (25OHD <50 nmol/L: median (interquartile range) = 47.7 (24.2) nmol/L). Vitamin D deficiency was greatest in those aged <50 years: median (interquartile range) = 43.3 (18.2) nmol/L, females: median (interquartile range) = 45.5 (19.4) nmol/L and those with higher educational qualifications: median (interquartile range) = 43.1 (18.7) nmol/L.

In the total Macau population, statistically significant ($p < 0.01$) modifiable associations with lower 25OHD levels were sunlight exposure ($\beta = 0.06$), physical activity (PA) (measured as hours(hrs)/day: $\beta = 0.08$), sitting (measured as hrs/day $\beta = -0.20$), intake of fish ($\beta = 0.08$) and calcium (Ca) supplement intake ($\beta = 0.06$) [linear regression analysis adjusting for demographic risk factors]. On similar analysis, and after adjustment for 25OHD, the only significant modifiable associations in the total population with PTH were sitting ($\beta = -0.17$), Body Mass Index ($\beta = 0.07$) and Ca supplement intake ($\beta = -0.06$).

In this Macau population less documented sun exposure, fish and Ca supplement intake and exercise were associated with lower 25OHD levels, especially in the younger population, along with the interesting finding that more sitting was associated with both lower 25OHD and high PTH blood levels.

In conclusion, unlike findings from Caucasian populations, younger participants were significantly more vitamin D deficient, in particular highly educated single females. This may indicate the desire of young females to be pale and avoid the sun. There are also big differences in lifestyle between the older generation and the younger, in particular with respect to sun exposure and PA.

This article is part of a Special Issue entitled '17th Vitamin D Workshop'.

1. Introduction

Established determinants of 25-hydroxyvitamin D (25OHD) status are exposure to sunlight and intake of vitamin D, either from foods or vitamin supplements [1–5]. Chinese populations have been found to be vitamin D deficient [6–23]. However, many of these studies were not sampled randomly from general population groups [11,13,14,18,19,22,23] and were from mainland China [9–11,14–17,19,20,22,23] (Table 1). In addition, there is discrepancy in the published data from China around the relationship between age and 25OHD levels. Several large studies from mainland China [8–10,17,19] reported that as the population aged, 25OHD levels reduced; these findings are consistent with data from Caucasian populations [1,24–26]. However, in other studies [13,16,20],

Abbreviations: 25OHD, 25-hydroxyvitamin D; PTH, parathyroid hormone; Ca, calcium; PA, physical activity; IPAQ-S, International Physical Activity Questionnaire short version; OR, odds ratios; 95% CI, 95% confidence intervals; SD, standard deviation; yrs, years; mins, minutes; hrs, hours; HK, Hong Kong; gen pop, general population; F, female; M, male; CPBA, competitive protein binding assay; RIA, radioimmunoassay; ECLIA, electrochemiluminescence immunoassay; OCTEIA, enzyme immunoassay; CLIA, chemiluminescent substances; HPLC, high performance liquid chromatography; 1,25D, 1alpha, 25(OH)(2) -vitamin D(3).

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increasing age was not found to be associated with lower 25OHD levels. It should be noted that three of the larger Chinese studies [9,17,19] investigated only elderly populations. This deficiency in Chinese populations has been hypothesized to be due to lack of sunlight [6,27,28]; however, none of the Chinese studies directly measured sunlight exposure (Table 1).

Again to our knowledge, few studies in China involving 25OHD analyses have investigated either dietary or supplement intake; one study estimated dietary Ca [10], and three dietary vitamin D [8,10,20], or Ca supplementation and milk consumption [8,10,20].

Thus, in this study in 2012 we aimed to investigate in the rapidly urbanizing city of Macau

1. the association between documented sun light exposure and dietary intake of vitamin D and Ca supplements and blood levels of 25OHD and PTH;
2. the association between exercise (both active and sitting) and blood levels of 25OHD and PTH;
3. these above associations (1 and 2) stratified by gender and age.

2. Material and methods

2.1. Study sample

A household-based random sampling design was used [29]. Five hundred and fifty-six blood samples were donated from participants aged from 19 to 84 in summer (August) 2012 in the city of Macau, China [4].

2.2. Data collection

A detailed interview-administered questionnaire documented demographics, sun exposure, and PA patterns, as well as intake of fish and vitamin D and Ca supplements. Sun exposure was measured by time spent in the sun (measured as self-reported minutes (mins) per day on weekends and weekdays in different seasons). In order to assess the levels of PA and sitting duration per day, the International Physical Activity Questionnaire short version (IPAQ-S) was used which contains objective questions regarding the frequency and duration of the PA [4]. Blood samples were collected and analyzed by electrochemiluminescence immunoassay (ECLIA 3) for both 25OHD (nmol/L) and PTH (pgms/mL) (Roche Diagnostics). The intra-assay coefficients of variation using control samples were 1.93% for 25OHD and 1.41% for PTH. The biochemical analyses were carried out at the Kiang Wu Hospital, Macau.

2.3. Data analysis

The sample was selected using a complex sample design where the study subjects were sampled with differential selection probabilities. Non-response and post-stratification adjustments were conducted to obtain the sample weights. Here, the sample weights are the number of observations in the population that can be represented by the sampled observations [30]. As a result, the selected sample is representative of the Macau population. Detailed sampling methods of the Macau survey are published elsewhere [29]. An initial descriptive data analysis (based on mean differences or correlation) was performed, and subsequent analytical analysis, to assess potential predictors of 25OHD levels by both linear and logistic regression analyses. 25OHD was positively skewed and was therefore log transformed or categorized depending on the type of analysis conducted; median and interquartile range were reported, along with untransformed means for ease of interpretation.

25OHD and PTH associations were assessed by correlation analysis (r^2) adjusted for demographic factors and graphing each value against each other, stratified by age using bubble plots with restricted cubic regression splines. The observations are represented by open circles (or bubbles) on the graphs where the areas of the circles are proportional to the sample weights of the observations. A restricted cubic regression spline analysis was conducted, with three knots specified at the 10th, 50th, and 90th quartiles. The algorithm for computing the sample-weighted spline variables and the use of sample weights in the plots for survey data is described in Korn and Graubard (1999) [30].

In the existing literature there have been conflicting results, with some studies finding younger participants having lower 25OHD [11,21] and others in the older populations [9,10,14,17,19,20] and also reporting females having lower 25OHD[11,13,14,16,17,22] and others not [9,19,23]. In our data, there were marked differences by age and gender for predictors of both 25OHD and PTH (e.g., fish, sun exposure); we thus tested for statistical interaction. This was assessed by the likelihood ratio test [31] in a saturated logistic model, including with main effects for age, gender, and interactions between age and fish consumption and sex and fish consumption and sex and age along with other risk factors. As these tests were significant ($p < 0.001$) for such interactions (see footnotes Tables 2 and 3), we subsequently stratified our analyses for gender and age. Multivariate adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were calculated [31] in order to establish the association between potential risk factors and vitamin D deficiency (25OHD < 50 nmol/L [1,26,32]), and higher PTH levels (PTH ≥ 60 pg/mL; mean + 1 standard deviation [SD]).

3. Results

3.1. Association between PTH and 25OHD

Figs. 1 and 2 are plots of 25OHD versus PTH values for people aged 50+ years ($r^2 = -0.24$, $p < 0.001$) and <50 years ($r^2 = -0.15$, $p < 0.001$), respectively. As can be seen from these graphs, there is a slight curve-linear association which is different by age category, but overall there is a slight negative correlation between the 25OHD and PTH ($r^2 = -0.18$, $p < 0.001$).

3.2. Prevalence of vitamin D deficiency and predictors of 25OHD levels

In this population from Macau, 25OHD median (interquartile range) was 47.7 (24.2), the mean 25OHD was 50.6 ± 17 nmol/L and the prevalence of vitamin D deficiency (25OHD < 50 nmol/L) was 55%. This varied demographically in that those who were younger (<50 years old) were 70% deficient; being female, 63% deficient; being college educated; 71% deficient; and being single, 80% deficient. These differences were reflected in the mean/median differences in 25OHD nmol/L (Table 2).

3.3. Lifestyle risk factors associated with 25OHD levels in total population

On linear regression analysis, adjusting for the above demographic risk factors, significant lifestyle associations with 25OHD levels were lack of sunlight exposure ($\beta = 0.06$, [95%CI: 0.04–0.09]), less mild PA (measured as hrs/day $\beta = 0.08$, [95%CI: 0.03–0.14]), more sitting (measured as hrs/day $\beta =$ [95%CI: –0.24- –0.16]), low intake of Ca supplements ($\beta = 0.06$, [95%CI: 0.03–0.09]), low intake of fish ($\beta = 0.08$, [95%CI: 0.02–0.14]). Body Mass Index (BMI) was not significantly associated with 25OHD ($\beta = 0.02$[95%CI: –0.15-0.19]).

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Table 1
Vitamin D (25OHD) and PTH studies in China 1989 – present.

Author, year	City, study sample	Gender (% male), Age	Sample size	Season, response rate	25OHD nmol/L mean ± SD/assay method	PTH mean ± SD pg/mL/assay method	Associations with ↓25OHD
Lau (1989) [13]	HK, 22.5°N community	50% male, 49–93 yrs	427	Summer-late autumn 100%	<70 F 62 ± 15 M 80 ± 25 ≥70 F 68 ± 17 M 80 ± 22 CPBA	36 ± 22 CLIA	No age difference, women
Yan (2000) [22]	Shenyang, 41.8°N factory workers	50% male, 25–75 yrs	194	Spring 100%	36 ± 16 RIA	31 ± 11 RIA	Women, PTH ≈25OHD
Woo (2008) [21]	HK 22.5°N Beijing, 40°N, gen pop	All young women, 20–35 yrs	221HK 220 Beijing	Late winter–spring 88%	HK: 34 (33-36) Beijing: 29 (27-30) RIA	HK: 34 (32-35) Beijing: 40(37-43) CLIA	No PTH ≈25OHD
Foo (2009) [11]	Beijing, 40°N, primary school	All women, mean 15 yrs	301	Late winter 86%	34 (32-35) RIA	36 (34-38) immunometric	PTH ≈25OHD, ↓muscle strength
Lu (2009) [17]	Beijing, 40°N, gen pop	44% male, 50–70 yrs elderly	3262	Spring 99%	40 (38-42) RIA	NA	Urban, women, ↑educat ,older, ↓PA winter
Chan (2012) [8]	HK, 22.5°N gen pop	100% male, mean 73 yrs elderly	939	Late winter 47%	78 ± 21 RIA	37(31-55) immunometric	↓PA, ↓diet vit D, ↑educat
Lu (2012) [16]	Shanghai, 31.1°N gen pop	26% male, 20–89 yrs	2588	Late winter 83%	M: 52 (47–67) F: 50 (40–60) ECLIA	Male: 31(24-42) female: 34(27-44) ECLIA	PTH ≈25OHD, ↓PA, ↓diet CA, women
Li (2012) [14]	Dali, 25.0°N factory workers	60% male, 20–83 yrs	1206	Spring 73%	55 ± 7 RIA	28 (26–34) CLIA	Older, women
Yin (2012) [23]	Jinan 36.6°N clinics	74% male, mean 49 yrs	601	Winter 100%	68 ± 26 RIA	NA	No gender difference
Lin (2012) [15]	Linxian, 36°N gen pop (farmers)	44% male, 40–69 yrs rural elderly	1101	Spring 99%	32 (20-48), OCTEIA	NA	No predictors,
Dorjgochoo (2012) [10]	Shanghai, 31.1°N gen pop	28% male, 40–75 yrs elderly	1460	Summer–autumn, 78%	35 (20-50) CLIA	NA	↑Age, winter, F:↓PA,↓ low diet vitamin D
Qiao (2013) [20]	Guiyang, 26.3°N gen pop	42% male, 40–59 yrs	1510	Late spring 100%	51 ± 23 RIA	32 ± 14 RIA	↑Age, ↑education, ↓PA,↓ milk, ↓Ca, (PTH ≈25OHD
Huang (2014) [12]	Taiwan, 25°N students	66% male mean 24 yrs	355	Summer–autumn 95%	73 ± 28 CLIA	NA	No predictors
Mao (2014) [19]	Shanghai, 31.1°N clinic patients	49% male, 67–99 yrs elderly	5470	Summer 100%	33 ± 20 HPLC	70 ± 33 μmol/L Immuno-assay	Winter, no gender difference, ↑age
Chen (2014) [9]	Beijing, 40°N gen pop	56% male,60–102 yrs elderly	1245	Late winter 77%	42 ± 16 CLIA	41 (13-103) ELICA	↑Age, no gender difference

Abbreviation: Ca, calcium; SD, standard deviation; HK, Hong Kong; gen pop, general population; F, female; M, male; CPBA, competitive protein binding assay; RIA, radioimmunoassay; ECLIA, electrochemiluminescence immunoassay; OCTEIA, enzyme immunoassay; CLIA, chemiluminescent substances; HPLC, high performance liquid chromatography; NA, not available; ≈, correlated with.

3.3.1. Risk factors associated with vitamin D deficiency (<50 nmol/L 25OHD)

Lifestyle factors associated with deficiency were having less than thirty mins of sun exposure per day compared to more (OR = 1.4, 95% CI:1.1–1.7); having low PA compared to moderate to high (OR = 1.8, 95% CI:1.5–2.2); sitting more than four hrs per day compared to less (OR = 1.6, 95% CI:1.3–2.0);taking Ca supplements less than once per week compared to more (OR = 1.5, 95% CI: 1.2–1.7); consuming fish less than four times per week compared to more (OR = 1.4, 95% CI:1.2–1.7).

3.3.2. Sub-group analyses (age and gender)

The above predictors varied markedly by age group and gender. Thus, the analysis was stratified by either age or gender: the tested interactions with various risk factors, 25OHD and either age or gender were highly significant ($p < 0.001$ for both) (Table 2).

3.3.2.1. Lifestyle risk factors in younger and older participants. In those aged less than 50 yrs, those having less than 30 mins of sun exposure per day compared with more were at a five-fold risk of deficiency (OR = 4.6, 95% CI:3.0–7.1); those who sat more than four hrs per day compared with less were at a three-fold risk (OR = 2.8, 95% CI:2.1–3.7); and those taking Ca supplements less than once per week and consuming fish less than four times per week were at three-fold risk of deficiency (OR = 2.5, 95% CI:1.5–3.9; OR = 2.6, 95% CI:1.9–3.7, respectively).

In contrast, the only factor predictive of 25OHD deficiency in those who aged more than 50 years was having low PA compared to moderate of high PA (OR = 1.8, 95% CI:1.3–2.5).

3.3.2.2. Lifestyle risk factors in females and males. Predictors of vitamin D deficiency in females were very similar to those for the younger population in that lack of sun exposure, more sitting, less intake of Ca supplements and fish all contributed to lower 25OHD levels (Table 2). In males, low dietary/nutrient intake (fish or Ca supplements) was not associated with 25OHD deficiency, but lack of sun exposure, low PA and more sitting all were associated with two-fold risk of deficiency.

3.4. High PTH blood values and lifestyle factor associations in total population

Lifestyle risk factors (significant linear associations with higher PTH) included higher Body Mass Index (BMI) (β = 0.07, [95%CI:

Table 2
Risk factors associated with 25OHD < 50 nmol/L in a population from Macau, China.

Risk factor distribution		25OHD			Young <50 yrs	Older ≥50 yrs	Female	Male
n = 566	%	Median (interquartile range)/mean (SD) nmol/L		OR[a] (95% CI)	OR[a] (95% CI)	OR[a] (95% CI)	OR[a] (95% CI)	OR[a] (95% CI)
Demographics								
Age (yrs)								
≥50	39	55 (26)	59 (18)	**1.0**			1.0	**1.0**
<50	61	43 (18)	45 (16)**	**1.8 (1.4–2.2)**			0.9 (0.6–1.3)	**1.7 (1.0–1.3)**
Education college								
No	78	50 (24)	52 (18)	**1.0**	**1.0**	1.0	**1.0**	1.0
College	22	43 (18)	44 (17)**	**1.4 (1.3–1.6)**	**1.8 (1.4–2.2)**	1.1 (0.8–1.2)	**1.5 (1.2–1.8)**	1.1 (0.9–1.3)
Marital status								
Married	83	50 (24)	53 (18)	**1.0**	**1.0**	**1.0**	**1.0**	1.0
Single	17	40 (16)	42 (15)**	**2.4(1.8–3.2)**	**2.9 (2.0–4.3)**	**0.2**(0.1–2.5)[b]	**2.7 (1.8–4.3)**	1.3 (0.9–2.0)[c]
Gender								
Male	38	52 (26)	56 (19)	**1.0**	**1.0**	**1.0**		
Female	62	45 (19)	47 (16)**	**2.6 (2.1–3.1)**	**2.5 (1.8–3.4)**	**2.4 (1.9–3.1)**		
Lifestyle								
Sun exposure								
≥30 mins/day	72	48 (23)	51 (18)	**1.0**	**1.0**	1.0	**1.0**	**1.0**
<30 mins	28	45 (26)	49 (17)*	**1.4 (1.1–1.7)**	**4.6 (3.0–7.1)**	1.2 (0.9–1.7)[b]	**1.5 (1.0–2.0)**	**1.6 (1.1–2.3)**
Physical activity								
Mod-high	75	51 (27)	55 (19)	**1.0**	1.0	**1.0**	1.0	**1.0**
Low	25	46 (22)	49 (17) **	**1.8 (1.5–2.2)**	0.6 (0.5–1.0)	**1.8 (1.3–2.5)**	0.9 (0.7–1.2)	**1.6 (1.2–2.3)**[c]
Sitting								
<4hrs/day	62	52 (26)	54 (18)	**1.0**	**1.0**	1.0	**1.0**	**1.0**
≥4hrs/day	38	44 (19)	46 (17)**	**1.6 (1.3–2.0)**	**2.8 (2.1–3.7)**	1.2 (0.9–1.5)	**1.8 (1.4–2.3)**	**1.6 (1.2–2.2)**
Diet and supplements								
Calcium supplements								
≥Once/week	14	55 (23)	56 (18)	**1.0**	**1.0**	1.0	**1.0**	1.0
<Once/week	86	47 (24)	50 (18)**	**1.5 (1.2–1.7)**	**2.5(1.5–3.9)**	1.1 (0.9–1.5)[b]	**1.8 (1.3–2.5)**	1.2 (0.7–1.9)[c]
Fish consumption								
≥4 times/week	71	48 (24)	51 (18)	**1.0**	**1.0**	1.0	**1.0**	1.0
<4 times/week	29	45 (24)	49 (18)**	**1.4 (1.2–1.7)**	**2.6(1.9–3.7)**	0.9 (0.6–1.1)[b]	**2.1 (1.6–2.8)**	0.9 (0.6–1.2)[c]

Abbreviations: OR, odds ratios; CI, confidence interval; yrs, years; mins, minutes; hrs, hours; *$p < 0.05$, **$p < 0.001$, OR in bold $p < 0.05$.
[a] OR values mutually adjusted for all other risk factors.
[b] $p_{interaction} < 0.001$, age × marital status, age × sun exposure, age × Ca supplements, age × fish.
[c] $p_{interaction} < 0.001$, sex × marital status, sex × PA, sex × Ca supplements, sex × fish.

0.02–0.12]), sitting more ($\beta = 0.15$, [95%CI: 0.08, 0.23]) and lower intake of Ca supplements ($\beta = -0.05$,)[95%CI: −0.08- −0.02].

3.4.1. Lifestyle risk factors associated with high PTH levels (≥60 pg/mL) in the total population

Lifestyle risk factors associated with high PTH levels were having less than thirty mins of sun exposure per day compared to more (OR = 1.7, 95% CI:1.2–2.4); and sitting more than four hrs per day compared to less (OR = 1.6, 95% CI:1.2–2.1).

3.4.2. Sub-group analyses (age and gender)

3.4.2.1. Lifestyle risk factors in younger and older participants. When stratified by age ($p_{interaction} = 0.002$), multivariate categorical analysis (including adjusting for serum 25OHD) associations with high PTH in the younger population were if they were married and had less than thirty mins of sun exposure per day compared to more (OR = 2.3, 95% CI:1.3–4.2); less than four hrs per day of moderate PA compared to more (OR = 1.5, 95% CI:1.0–2.3); sitting more than four hrs per day compared to less (OR = 1.5, 95% CI:1.3–2.2); were obese compared to not (OR = 7.8, 95% CI:4.6–13); and consumed more Ca supplements compared to less (OR = 0.5, 95% CI:0.2–0.8). In contrast, those who were older were at risk of higher PTH levels only if they were female (OR = 1.8, 95%CI:1.2–2.8) and sat more than four hrs per day compared to less (OR = 1.8, 95% CI:1.1–2.6) and did not take Ca supplements more than once per week compared to more (OR = 4.3, 95% CI:2.0–9.5).

3.4.2.2. Lifestyle risk factors in females and males. When stratified by gender ($p_{interaction} = 0.002$), females were at risk for higher PTH if they had less than thirty mins of sun exposure per day compared to more (OR = 2.7, 95% CI:1.7–4.5); sat more than four hrs per day compared to less (OR = 1.9, 95% CI:1.3–2.7) and were obese compared to not (OR = 2.5, 95% CI:1.6–4.0).

In contrast, males were only at risk if married and had less than four hrs per day of moderate PA compared to more (OR = 1.9, 95% CI:1.2–3.2) and were obese compared to not (OR = 4.0, 95% CI: 2.2–7.4).

4. Discussion

In summary, in our data those who were either younger, female, or college educated had 25OHD deficiency. The predictors of this deficiency varied markedly by age and gender, with less sun light exposure, fish consumption and Ca supplement intake and more sitting predicting deficiency in those aged less than fifty years. In the older population, less PA was the only significant predictor of deficiency. There was a marked difference by gender; in females,

Table 3
Risk factors associated with high PTH (≥60 pg/mL) (adjusted for 25OHD) in a population from Macau, China.

Risk factor distribution		PTH		Young <50 yrs	Older ≥50 yrs	Female	Male
n = 566	%	pg/mL	OR[a] (95% CI)	OR[a] (95% CI)	OR[a] (95% CI)	OR[a] (95% CI)	OR[a] (95% CI)
Demographics							
BMI							
<28	88	42 (18)	**1.0**	**1.0**	1.0	**1.0**	**1.0**
≥28	12	44 (16)**	**2.9 (2.0–4.1)**	**7.8 (4.6–13)**	1.4 (0.8-2.6)	**2.5 (1.6–4.0)**	**4.0 (2.2–7.4)**
Age (yrs)							
≥50	39	44 (15)	1.0			1.0	1.0
<50	61	44 (17)	1.1 (0.8–1.5)			0.8 (0.6–1.2)	1.7 (0.9–2.9)
Education							
No	78	44 (16)	1.0	**1.0**	1.0	1.0	1.0
College	22	44 (18)	1.1 (0.8–1.5)	**1.6 (1.0–2.4)**	0.6 (0.2–1.4)	0.9 (0.6–1.3)	1.1 (0.8–1.6)
Marital Status							
Married	83	44 (15)	**1.0**	**1.0**	1.0	1.0	**1.0**
Single	17	43 (21)**	**0.6 (0.4–0.9)**	**0.5 (0.3–0.9)**	0.7 (0.3–2.4)	0.6 (0.4–1.0)	**0.4 (0.2–0.9)**
Gender							
Male	38	43 (14)	**1.0**	1.0	**1.0**		
Female	62	45 (18)**	**1.4 (1.0–1.9)**	1.4 (0.9–2.1)	**1.8 (1.2–2.8)**		
Lifestyle							
Sun exposure							
≥30mins/day	72	44 (17)	**1.0**	**1.0**	1.0	**1.0**	1.0
<30mins/day	28	42 (12)*	**1.7 (1.2–2.4)**	**2.3 (1.3–4.2)**	0.8 (0.5–1.4)	**2.7 (1.7–4.5)***	0.7 (0.4–1.3)[c]
Physical activity							
Mod-high	75	44 (17)	1.0	**1.0**	1.0	1.0	**1.0**
Low	25	43 (15)	1.2(0.9–1.7)	**1.5(1.0–2.3)**	1.0 (0.6–1.7)	1.0(0.7–1.6)	**1.9 (1.2–3.2)**
Sitting							
<4hrs/day	62	42 (14)	**1.0**	**1.0**	**1.0**	**1.0**	1.0
≥4hrs/day	38	47 (19)**	**1.6 (1.2–2.1)**	**1.5 (1.3–2.2)**	**1.8 (1.1–2.6)**	**1.9 (1.3–2.7)**	1.4(0.9–2.3)
Diet and supplements							
Calcium supplements							
≥Once/week	14	44 (17)	1.0	**1.0**	**1.0**	1.0	1.0
<Once/week	86	42 (13)*	0.9 (0.6–1.3)	**0.5 (0.2–0.8)**	**4.3(2.0–9.5)**[b]	0.9(0.6–1.5)	2.2 (0.7–6.6)
Fish consumption							
≥4 times/week	71	44 (16)	1.0	1.0	1.0	1.0	1.0
<4 times/week	29	43 (17)	1.2 (0.9–1.6)	1.3 (0.8–2.0)	0.9 (0.6–1.4)	1.0 (0.7–1.4)	1.1 (0.6–1.8)

Abbreviations: OR, odds ratios; CI, confidence interval; yrs: years; mins: minutes; hrs: hours; * $p < 0.05$, ** $p < 0.001$, OR in bold $p < 0.05$

[a] OR values mutually adjusted for all other risk factors and 25OHD levels.
[b] $p_{interaction} < 0.001$, age × Ca supplements.
[c] $p_{interaction} < 0.001$, sex × sun exposure.

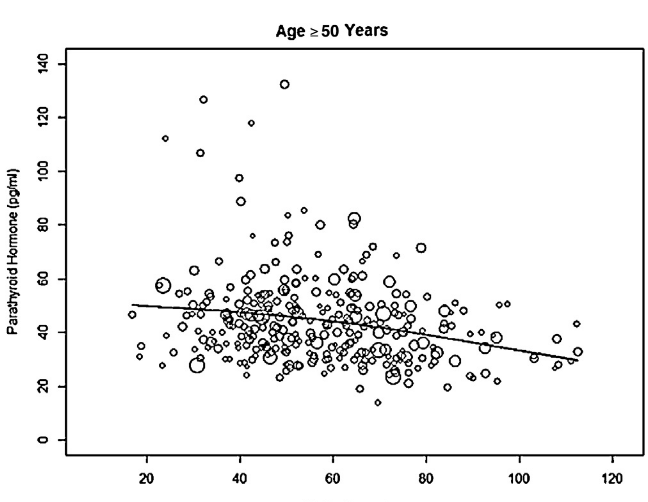

Fig. 1. The association between 25OHD and PTH levels in elderly (≥50 years old) from a population in Macau, China 2012.

sun exposure, dietary intake and sitting were associated with deficiency, whereas in males, less sun exposure, more sitting and less PA were predictors of deficiency.

4.1. Vitamin D deficiency; comparison to other Chinese populations

4.1.1. Prevalence of deficiency

The Macau results from the present study for vitamin D status (mean = 50.6 ± 17 nmol/L) were closer to, but a little lower than, those reported from cities of similar latitude, such as Hong Kong (HK) and Taiwan. Values reported from HK and Taiwan averaged 64 ± 20 nmol/L and ranged from 34 nmol/L in young women in HK [21] at the end of winter to 78 nmol/L in HK males in summer [13]. In contrast, the Macau results were higher than those reported from mainland China (averaging 43 ± 12 nmol/L) ranging from 29 nmol/L in young women in Beijing at the end of winter [21] to 68 nmol/L in Jinan clinics in summer [23] (Table 1).

4.1.2. Sunlight exposure, dietary vitamin D and supplement intake

Sunlight exposure and food and supplement intake are known and well established predictors of 25OHD and have been consistently reported [1,2,5,24–26,32,33]. To our knowledge, no

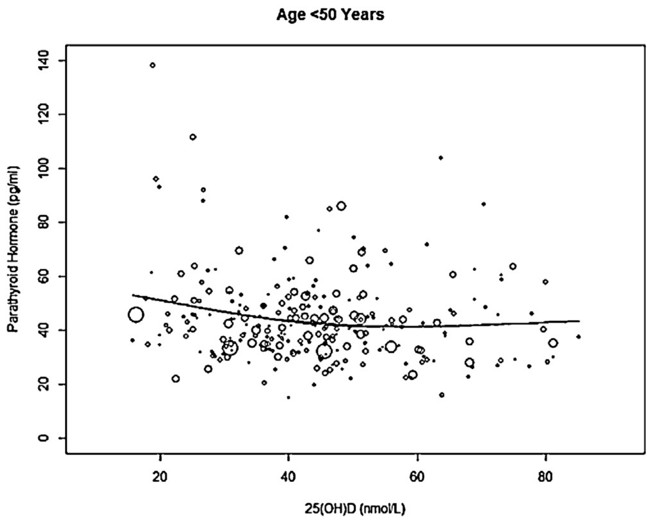

Fig. 2. The association between 25OHD and PTH levels in younger (<50 years old) from a population in Macau, China 2012.

study attempted an estimation of sun exposure, as was measured in our questionnaire. In studies from China, it appears that season was accounted for in very few studies [10,17], although most restricted their blood draw to one season. In a previous publication on a larger data set ($n = 1410$) from this population, we reported that increased sunlight exposure and fish consumption were associated with less hypertension and hypothesized that these measures may be good surrogates for 25OHD levels in blood, although sunlight itself may have an effect on hypertension [4].

It should be noted that, few studies in China have investigated either dietary or supplement intake involving 25OHD analyses. In our study, dietary intake appears to be more important in women. This is complemented by a parallel study focusing on dietary patterns, where authors analyzed data from the 1995–96 Hong Kong Dietary Risk Prevalence survey in adult Chinese aged 25–74, where single women had lower nutrient densities of vitamin D as well as iron, and ate more fruits and vegetables than married women [34]. A recent study of Singaporean Chinese reported data on dietary and other lifestyle factors in 504 older participants and also found 25OHD associated with dietary vitamin D, calcium, and dairy product intake among women, but not among men [35].

These interesting gender and age differences in vitamin D status and dietary and supplement intake need to be investigated more fully in human feeding studies in East Asian populations.

4.1.3. Exercise and sedentary behavior: "Newer" predictors of vitamin D deficiency

Along with this present study and four studies from China [10,16,17,20], epidemiological studies have consistently found leisure time PA to be a contributor to vitamin D status [1–3,25,33,36–38]. This association has often been attributed to PA being a surrogate for sun exposure; however, in the few studies in which both exposures were measured simultaneously [36,39,40], the PA-vitamin D relationship persisted independently of sun exposure. Maybe some aspect of exercise is contributing to the maintenance of vitamin D status, other than by increasing exposure of skin to sunlight, as suggested by recent *in vivo* and *in vitro* studies [41,42].

A mechanism of action has been suggested in studies by Abboud et al. [41] who report that specific uptake of 25OHD into muscle may contribute to the long half-life of 25OHD in blood, and that exercise may further extend the time that 25OHD molecules can circulate in blood without being degraded.

It is known that proximal muscle weakness (myopathy) associates with nutritional osteomalacia (caused by severe vitamin D deficiency) and is responsive to supplementation with vitamin D [43]. Despite these hypotheses, recent reviews have presented conflicting evidence from human randomized control trials of 25OHD supplementation and muscle strength, gait and balance [44–46].

Recent meta-analyses of sedentary behavior [47] have found that sitting is a very good predictor of sedentary behavior patterns, although little work on this relationship has been reported from Asian countries. The epidemiological associations that we have reported between more sitting and lower 25OHD levels have also been reported by Robien et al. in Singapore [35], but to our knowledge have not been reported elsewhere in the literature.

Further investigation into the role of PA and sitting, independent of sunlight exposure in vitamin D metabolism, would appear warranted.

4.2. Sub-group analyses (age and gender)

4.2.1. Age

In contrast to the general trends reported in China (Table 1), in our data we have reported those aged greater than 50 years have higher 25OHD levels than their younger counterparts. It should be noted that this present population had a wide age range from 18 to 93, with a mean of 47 ± 17 and 61% were aged less than 50. We hypothesize that these results are reflecting a rapid "westernization" of Macau, with the younger participants taking on a lifestyle of more indoor work habits compared to their elders who still enjoy outdoor activities.

4.2.2. Gender

In our data, and our studies in Australia [6,36] and those reported in China [13,14,16,17,22], women tended to have lower 25OHD levels than men, especially younger women [11,21]. We have previously reported in a qualitative study, examining attitudes in Chinese women living in Australia, that a number of cultural factors played an important role in forming negative attitudes toward sun exposure among participants, including fair skin preference, a cover-up tradition, the non-existence of sunbathing culture, and an indoor lifestyle [27]. A survey in HK suggested that East Asian women often deliberately avoided sunlight as they traditionally preferred "fair skin". In many East Asian countries where Buddhism and Confucianism are the predominant philosophies, the idealization of fair skin especially for women has a long history, and a fair complexion is an indication of beauty, privilege, social status, and femininity. In the past, those from poor, working class families who had to work in the sun had rough, tanned skin and thus fair skin was seen as "aristocratic" and became a sign of higher status. In the present day, it is thought that such ideas are more related to standards of beauty, i.e., whiter skin is the desired beauty goal [28].

4.3. Parathyroid Hormone

An analysis of our data has reported an association between 25OHD and PTH, which has also been investigated in the majority of Chinese studies [8,11,14,16,19–22,27]. Although it is difficult to compare these studies due to differing assay methods, our values (mean 44 ± 16 pg/mL range 14–138) appear to be similar to those reported (Table 3). As has been reported in a recent meta-analysis [48], there is huge variation in the correlations between 25OHD levels and PTH levels, varying from none [21] to very weak [22] to stronger [9,19]. At least part of this variability is because the two major repressors of PTH secretion are blood Ca concentrations and 1alpha, 25(OH)

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(2)-vitamin D(3) (1,25D). The active vitamin D hormone can be made in the parathyroid gland, depending on 25OHD availability [49] and directly represses PTH gene transcription [33]. Ca concentrations, which directly affect the Ca sensing receptor in the parathyroid gland, depend at least in part on Ca intake as well as on circulating 1,25D concentrations, since this hormone modulates active calcium absorption from the gut. PTH has recently been linked to mortality and cardiovascular outcomes [50]. The strong PTH-BMI association in our data is consistent with these findings.

To our knowledge, our reported demographic and lifestyle associations with higher PTH levels are somewhat new and provocative. While 25OHD concentrations are important determinants of PTH concentrations, calcium intake is a known independent variable affecting PTH [51]. We have no indications as to why sun exposure might independently affect PTH concentrations but speculate that it may be related to nitric oxide release or some other non-vitamin D dependent effect of sunlight [52]. We have no suggestions as to why there is an independent effect of sedentary behavior on PTH, an observation that warrants investigation in other cohorts.

4.4. Strengths and limitations

The strengths of the present investigation are the representativeness (random sample) of the study population. In addition, this is the first time to our knowledge that direct measures of sun exposure and sitting have been measured in China. It should be noted that these samples are from the 60% who volunteered to give blood from the larger randomly selected population surveyed [4]. This is somewhat lower than the mean response rates reported from similar Chinese studies (Table 1), which ranged from 47% to 100% and, as such, there may be bias due to this response rate. However, when this present sample was compared to the parent data [4], there was little difference in demographic variables investigated, except that those who donated blood samples had a slightly higher distribution of married participants (5% more married than in the original sample) and more women compared to men (6% more women than in original sample). It should be noted that our study is also limited by being cross-sectional. In addition there was no direct measure of PA, sitting or sun exposure.

5. Conclusion

The major new findings of this study in Macau are that younger participants are significantly more deficient in vitamin D, in particular highly educated single females. This may indicate the desire of young females to be fair-skinned and thus avoid the sun. It also seems that there are big differences in lifestyle between the older generation and the younger, in particular with respect to sun exposure and PA; further investigation of these patterns is warranted. It is very interesting and new that sitting, independent of sun exposure, may be a potentially modifiable independent risk factor for protecting against vitamin D deficiency in this population.

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