No Correlation between 25-Hydroxyvitamin D status and pro or anti-inflammatory cytokines in obese children and normal weight controls

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Background

- The primary function of vitamin D relates to calcium and bone metabolism but it is now recognised that vitamin D is a potent immunomodulator.
- In vitro, 1,25$(OH)_2$D has been shown to suppress pro-inflammatory cytokines, such as TNF-α and IL-6, while up regulating synthesis of anti-inflammatory cytokines, IL-10 and IL-4 [1,2]. There are no in vivo studies examining the relationship between 25-Hydroxyvitamin D (25OHD) and cytokines in healthy children.
- Obesity is recognised as a pro-inflammatory state, characterised by higher levels of TNF-α and IL-6 and lower levels of adiponectin[3].
- Obese individual are also more likely to be vitamin D deficient.

Aim

- To examine if vitamin D status altered the cytokine profile in different groups of children; obese children and lean healthy control children.
- The secondary aim was to determine if the cytokine profiles differed between obese and lean children.

Materials and Methods

Over a 12 month period 2 groups of children in a paediatric hospital were recruited;

- obese children (BMI > 98th centile) attending a weight management course
- healthy children attending the hospital for minor medical or surgial illnesses.

Each had 25OHD level measured along with a cytokine panel (TNF-α, IL-4, IL-6, IL-10 and adiponectin).

Results

- In the obese cohort there were 13 children (9 females) ranging in age from 7.6-15.8 years. The mean (SD) 25OHD level was 29.2 (17.0) nmol/L and 92% had 25OHD levels <50 nmol/L.
- There were 46 *healthy* children (28 females) ranging in age from 4.4-15.6 years. The mean (SD) for 25OHD was 44.7(24.6) nmol/L and 54% had 25OHD levels <50 nmol/L.
- There was no correlation between the cytokines examined and 25OHD levels in either group (Table 1 and Figure 1).
- 25OHD levels and cytokine profiles differed significantly between the two groups (Table 2).

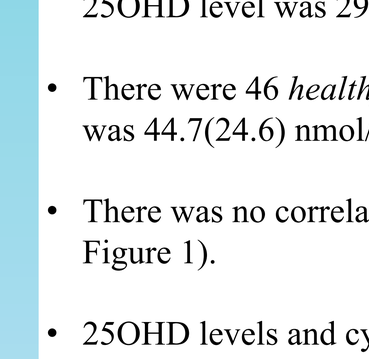
Table 1 : Correlation between 25OHD levels and cytokines in obese children

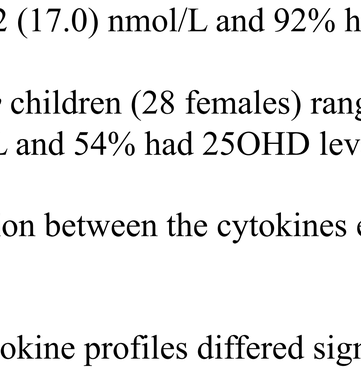
	Mean (SD)	r-value	p-value
IL-10 (pg/ml)	2.4 (1.7)	0.065	0.760
IL-4 (pg/ml)	2.9 (2.8)	-0.119	0.579
IL-6 (pg/ml)	0.99(0.70)	0.194	0.359
TNF-α (pg/ml)	7.6 (2.8)	0.199	0.516
Adiponectin (ug/ml)	70.07(11.85)	0.312	0.299

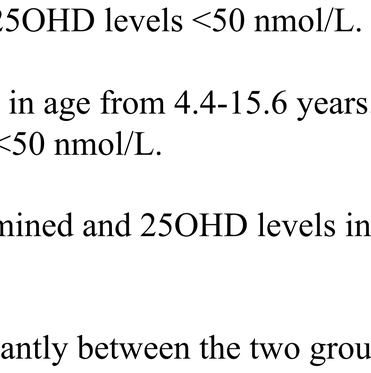
Table 2 : Comparison of 25OHD and cytokines levels between healthy and obese subjects

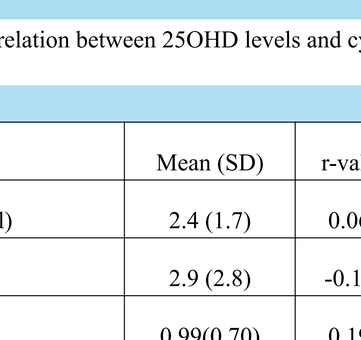
	Healthy (n=46)	Obese (n=13)	p-value
25OHD (nmol/L)	44.7(24.6)	29.2 (17.0)	0.038*
IL-10 (pg/ml)	1.23(2.05)	2.21(2.74)	0.210
IL-4 (pg/ml)	0.51(3.12)	2.98(4.55)	0.106
IL-6 (pg/ml)	0.08(0.43)	1.01(1.17)	<0.001*
TNF-α (pg/ml)	5.6(+/-1.8)	7.6(2.8)	0.005*
Adiponectin (ug/ml)	100.1(+/-14.6)	70.0(11.8)	<0.001*

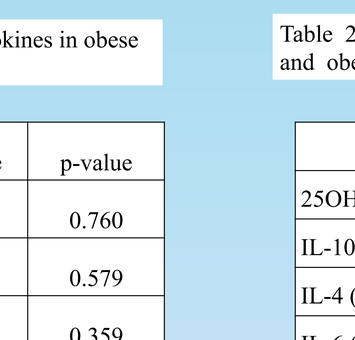
Figure 1 : Correlation between 25OHD levels and cytokines in healthy children











Discussion

- We believe this is the first study examining the relationship between 25OHD status and pro and anti-inflammatory cytokines in healthy children. We found no correlation. There are a number of possible explanations for this.
- Firstly, the 25OHD levels of our patients were possibly below the threshold required for 25OHD to exert it's immunomodulatory effects. Zhange et al demonstrated a level of 75 nmol/L was required to successfully inhibit TNF-α and IL-6 production[4].
- Secondly, our patients were in good health at the time of sampling and a correlation between 25OHD and cytokines may only be evident when the immune system is stimulated through sepsis or disease.
- Thirdly, 1,25 $(OH)_2$D is the active form of vitamin D which exerts an influence on immune cells and this was not measured in our study.
- We found no correlation between 25OHD status and cytokine profiles of obese children. Previous studies have yielded inconsistent results.
- We did find a significant difference in pro-inflammatory cytokines when obese and lean controls were compared. Adipocytes possess vitamin D receptors and express 1α-hydroxylase and 1,25$(OH)_2$D has been shown to affect cytokine expression in adipocytes making it plausible that vitamin D status may be a factor in the pro-inflammatory state seen in obesity[5].
- In conclusion, we found no correlation between 25OHD and either pro or anti-inflammatory cytokines in healthy or obese children. We did demonstrate a pro-inflammatory state in the obese cohort.

References

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