Pakistanis living in Oslo have lower serum 1,25-dihydroxyvitamin D levels but higher serum ionized calcium levels compared with ethnic Norwegians.

The Oslo Health Study.

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1. Is the question posed by the authors new and well defined?
The objective of this research was to investigate whether Pakistani immigrants living in Oslo have an altered vitamin D metabolism by means of compensatory higher serum levels of 1.25-dihydroxyvitamin D compared with ethnic Norwegians and secondly whether serum levels of ionized calcium differ between Pakistanis and Norwegians. This is a sound research question in view of how common vitamin D deficiency and elevated serum parathyroid hormones are in immigrants in Norway. Previous studies in different ethnic groups and age groups have been conflicting in terms of the relationship between concentration of 25-hydroxyvitamin D and 1.25 dihydroxyvitamin D although most of them have showed a positive precursor-product relationship.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
The study group consists of a limited number of 94 Pakistani men and 67 Pakistani women, aged 30-60 years (29% of the originally invited group, women 42%) compared to a larger number of 290 Norwegian men and 270 Norwegian women, age 45-60 years (46% of the original group, women 48%). The recruitment period was from May 2000 to January 2001 but it is not described further if the recruitment was equally distributed for the Pakistanis and Norwegians over this time period. The authors mentioned that three subjects were excluded (Norwegians or Pakistanis?) due to primary hyperparathyroidism as defined by S-iPTH >8.5 pmol/L and serum ionized calcium >1.35 mmol/L. This level of ionized calcium of 1.35 mmol/L is rather high and does not therefore exclude some borderline primary hyperparathyroid patients with ionized calcium in the upper range and PTH also within normal limits but inappropriately high. Just a few such cases could affect the relationship between ionized calcium and PTH levels which is the main finding of this paper. The authors should therefore describe better the distribution of ionized calcium and PTH level within the study group to exclude any possible difference between the study groups in this respect. This is only partly done by Figure 1.

3. Are the data sound and well controlled?
The blood sample collected from each participant on the day of attendance was a non-fasting one which might be a limiting factor in studying the relationship between ionized calcium and PTH as post prandial fluctuations in ionized calcium are likely to occur to some extent followed by PTH changes. The authors might therefore mention this in the discussion as a possible limitation.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes, in most respect. As mentioned previously it might be useful to have the range of the variables in Table 1.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
The data certainly support the conclusion made by the authors that this Pakistani group does not seem to compensate for their vitamin D deficiency by increasing their production of 1.25-dihydroxyvitamin D. The other main finding is higher ionized calcium at any PTH level amongst the Pakistanis. The authors do not claim that they have the explanation for this but suggest that the Pakistanis have a higher set point of calcium. They mention that the differences may be due to lifestyle factors such as a dietary acid load changing serum pH or a combination of several factors. As the blood samples were not collected fasting and the groups might have attended at different hours after meals, this might affect the results and the
authors should address this possible problem in the design of the study. At the end they mention that the implications of higher serum calcium for bone metabolism and bone health in Pakistani immigrants need to be further studied presumably referring to their previous finding that the bone mineral density amongst the Pakistanis is similar to the ethnic Norwegians with different vitamin D status.

6. Do the title and abstract accurately convey what has been found?
Yes.

7. Is the writing acceptable?
The manuscript is on the whole clearly written in good English.