Masterjohn May 15

Yesterday the very first COVID-19 study using pre-infection vitamin D status was released as a preprint.*

Using data from the electronic health records of patients treated at University of Chicago Medicine, of the 4,314 people who were tested for COVID-19, 499 had their vitamin D status measured in the year before the COVID-19 test, excluding the 14 days prior to the test. The is the very first study that has taken the vitamin D status measurements prior to the COVID-19 test, and the fact that they excluded the 14 days leading up to the test suggests that they almost always obtained pre-infection levels.

This is critical because getting infected with COVID-19 most likely decreases vitamin D status, and up to now there has been no basis for suggesting that vitamin D status prior to getting infected drives the risk of getting infected or the severity of the ensuing infection.

This study still has no power to assess cause and effect, but it increases the plausibility that vitamin D status affects infection risk because in order for one thing to cause another, the cause must come first.

Strangely, the authors grouped in seven patients whose vitamin D status was measured as calcitriol, the active hormonal form of vitamin D, with the rest of the patients who had their vitamin D status measured as 25(OH)D, the standard measurement. In my opinion they should have kept these patients separate.

Vitamin D status was considered deficient with a 25(OH)D under 20 ng/mL or a calcitriol level under 18 pg/mL.

With deficient vitamin D status, the risk of a positive COVID-19 test was 19%. With 25(OH)D between 20-29.9, the risk was 13%. For 30-39.9 the risk was 11%. For 40-100, the risk was 12%. These differences did not reach statistical significance even when the deficient group was compared to the others (p=0.11).

Then they performed a more complex analysis. They defined anyone who was deficient on vitamin D testing and did not have their vitamin D dose increased as “likely deficient” at the time of COVID-19 testing, and defined everyone who was not deficient and did not have their vitamin D dose decreased as “likely sufficient.” Everyone else was considered “uncertain.” When they statistically adjusted for age, gender, race, Hispanic ethnicity, BMI, hypertension, diabetes, chronic pulmonary disease, pulmonary circulation disorders, depression, immunosuppression, and markers of liver disease and chronic kidney disease, those who were

“likely deficient” had a 77% higher risk of a positive test than those who were “likely sufficient” ($p<0.02$).

That such an enormously complex model is needed to show statistical significance indicates that the association between pre-infection vitamin D status and a positive COVID-19 test is very weak.

There was no association with whether the most recent dose of vitamin D someone was taking was up to 1000 IU, 2000 IU, or equal to or greater than 3000 IU.

This continues a trend I had identified in my analysis of the second and third vitamin D studies: “As more studies continue to roll in, it may be the case that the association becomes more and more robust, but the strength of the association becomes weaker than it looked from the first two papers. In other words, it becomes clearer and clearer that vitamin D is relevant, but less and less likely that it is some kind of magic bullet.”

These data suggest that staying out of the deficient zone of 20 ng/mL reduces infection risk about 42%, but little is done with levels higher than that.

I still support maintaining 30-35 ng/mL, because this appears to be the sweet spot for what to maintain during the course of the disease to prevent it from becoming severe or fatal, assuming the associations are cause-and-effect relationships, which has yet to be demonstrated.

There is no evidence of a U-shaped curve from this study, even though 76 of the patients had 25(OH)D between 40 and 100 ng/mL. However, they do not provide the mean, median, range, or standard deviation within this group, so they give no sense of how the data points are distributed within it. Hopefully, peer reviewers will encourage these authors to include a box-and-whiskers plot with individual data points, which provides the most information about how the data are distributed within each group. Given how little we know about the data distribution in the 40-100 ng/mL range, I am not yet relieved of my concern about a possible U-shaped curve.

The first pre-infection study makes the association less impressive than it had been in the one other study on infection risk, where the median time of vitamin D testing was 3 days after the COVID-19 test. Nevertheless, it supports my current position of maintaining 30-35 ng/mL, which may represent the ideal range for the combined set of concerns of maintaining low infection risk, and restraining an infection, if one develops, from becoming severe or fatal.

By the way, here are my other posts on vitamin D and COVID-19 so far:

- My Response to Rhonda Patrick on Vitamin D and COVID-19
- Update on Vitamin D and COVID-19 Using the First Observational Study Released

- The Second Study on Vitamin D and COVID-19 Is Now Out
- Two New Vitamin D Studies
- Vitamin D: The First Study on COVID-19 Infection Risk