Clinical Chemistry

Serum Total Testosterone Concentrations in the US Household Population from the NHANES 2011–2012 Study Population

Article:
H. Vesper *et al*.
Serum Total Testosterone Concentrations in the US Household Population from the NHANES 2011–2012 Study Population.
Clin Chem 2015;61:1495-1504
http://www.clinchem.org/content/61/12/1495.abstract

Guest:
Dr. Herbert Vesper is the Director of Clinical Standardization Programs and the Chief of the Protein Biomarker Laboratory at the CDC in Atlanta.

Bob Barrett: This is a podcast from *Clinical Chemistry*, sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

Testosterone is a key hormone for the regulation of sexual differentiation and development. Testosterone could affect the metabolism of blood lipids and glucose and serum concentrations of testosterone are associated with cardiovascular disease, diabetes, osteoporosis, and other conditions.

Despite the increasing use of testosterone measurements in patient care and research, only limited information is available about testosterone concentrations in the general US population, especially women and children.

In the December 2015 issue of *Clinical Chemistry,* a paper examines serum total testosterone concentrations in the US population. The senior author of that article is Dr. Herbert Vesper. He is the Director of Clinical Standardization Programs and the Chief of the Protein Biomarker Laboratory at the Centers for Disease Control and Prevention in Atlanta. And he is our guest in today's podcast.

Dr. Vesper, first of all, tell us what is NHANES and why is it important?

Dr. Herbert Vesper: Well, NHANES is a program of studies designed to assess the health and nutritional status of adults and children in the United States. And this survey is unique because it combines interviews, physical examinations and laboratory tests on a broad range of biomarkers, and it is the only survey that provides national representative health data.

Now NHANES started in 1960, and became a continuous ongoing survey in 1999. It is a cross-sectional survey that is repeated every two years, and with that it allows for the assessment of differences in health status and biomarker levels in the US population across different surveys, and

then these differences are indicative for trends in the US population.

Now, in this context one has to keep in mind that the data we show are national representative, which means they do not represent normal ranges that people sometimes use to distinguish healthy people from the people with certain diseases. However, the NHANES data can be used to determine the prevalence of certain diseases using established clinical decision levels. And in our study we described new national representative data on serum testosterone in the general US population for the years 2011 and 2012.

Bon Barrett: So you mentioned new data in the study, tell us about the new data in the study that you just published in *Clinical Chemistry*.

Dr. Herbert Vesper: Okay, well national representative data on testosterone levels were reported in earlier NHANES surveys; however, these measurements were limited to men, did not provide information on Asian-Americans or children. Our study now provides for the first time national representative data for children aged 6 years and older, women, and Asian-Americans.

Bob Barrett: Did you see any difference among race or ethnic groups?

Dr. Herbert Vesper: Yes, we did. We observed differences in total testosterone values among race, ethnic groups in male participants, but not female participants; and these differences were not consistent for children and adults. So compared to other race ethnic groups covariate-adjusted total testosterone values in non-Hispanic Asians were higher among children, but lowest among men.

The other observation was that testosterone concentrations were higher in Mexican-Americans than non-Hispanic white men, and these differences probably need to be considered when generating reference ranges and using reference ranges in the clinical context to evaluate patients.

Also we observed for the first time a peak in covariate-adjusted total testosterone values in men around age 60, and this pattern was not reported in previous NHANES surveys. In these surveys a decline in testosterone value with increasing age was observed.

Now the reason for these differences in pattern in the US population is not known and needs further investigation. However, in reports by other investigators does mention a profound increase in the use of androgen therapy in men over the past couple of years.

Unfortunately information about androgen use is not available for this NHANES survey. However, our data most likely include patients on androgen therapy which may explain the higher covariate-adjusted total testosterone values that we see in people of age 60. Also when we look at unadjusted percentiles, the pattern I just described is only observed in the higher percentiles but not in the lower percentiles.

Individuals in the higher percentiles most likely include patients on androgen therapy, which seems to support this hypothesis of increased testosterone levels due to increase of androgen therapy. But as I said, further investigations are needed to verify this hypothesis.

And furthermore, our findings such as that fasting status in addition to diurnal variation seems to affect total testosterone levels. So specifically we found that total testosterone value is consistently lower in non-fasting compared to fasting adults, independent of the type of specimen collection.

And fasting status show different associations between total testosterone and BMI in women, and total testosterone and smoking status in men. In the past diurnal variation was considered the only major biological factor affecting testosterone levels.

Now our findings suggest that additional studies on the impact of fasting status on total testosterone levels are needed to better determine the importance of fasting on testosterone levels.

Bob Barrett: Doctor, how did the measurements performed in this study differ from those in previous studies?

Dr. Herbert Vesper: The measurements performed in previous NHANES studies were performed using an immunoassay found by other investigators to be inaccurate especially at low concentrations typically observed in women and children. The data reported in our study were generated using mass spectrometry-based method standardized to CDC's standardization program, which means it has a high level of accuracy and precision and is traceable to a general accepted reference basis.

Specifically our method showed a precision of less than 4.8% determined from data collected over a period of two years. It has a limit of detection of 0.28 ng/dL, it shows no significant difference to establishment of logical reference methods.

One of the advantages of having this method standardized to CDC standardization programs is that data produced by our method can easily be compared to data produced by other assays, also standardized to the CDC standardization program, and this was not possible before.

So, for example, if another laboratory with a standardized method wants to know how their data compares to the national average, they can easily perform such a comparison using the data mentioned in our study.

Bob Barrett: Since the CDC is monitoring the US population over so many years, how do you deal with changing analytical methods over the decades?

Dr. Herbert Vesper: Well, changing analytical methods in multiyear studies can result in changes in measurement accuracy. As a consequence, shifts in data can be observed suggesting shifts in biomarker values in that particular study population, while in fact the shift is solely related to changes in the analytical method.

This is a problem for all longitudinal studies, not just NHANES and the investigators need to be aware of that potential problem.

Now the problem can be addressed and resolved through standardization programs that monitor measurement accuracy over time. An example is, CDC standardization programs provide samples with target values assigned by a reference method, and the principal investigators can add these samples to their study as blind quality control samples for example, and monitor the accuracy over long period of times.

At the same time, laboratories can participate in these programs, for example, the CDC has Lipid Standardization Program, and there they can monitor the performance themselves over long periods of time. And these approaches have successfully been used for blood lipids, and are currently available also for testosterone, estradiol, and vitamin D.

Bob Barrett: Would it be better to not change methods and have the same slightly wrong answer and consistency, or is it better to always have the most accurate method available even though that changes over time?

Dr. Herbert Vesper: If there is an accuracy basis available, it is recommended by organizations such as DASST and other groups to link measurements to that accuracy basis.

Now, methodologies can change, technology can change over time, and we need to accommodate these changes. However what we want to do is we want to make sure that the measurement is accurate, independent of the technology being used.

And so standardization programs can provide this sort of accuracy assessment to ensure that measurements are accurate over time, independent of the technology being used.

Bob Barrett: Dr. Herbert Vesper is the Director of Clinical Standardization Programs and the Chief of the Protein Biomarker Laboratory at the CDC in Atlanta. He has been our guest in this podcast from *Clinical Chemistry* on testosterone concentrations in the US population.

I am Bob Barrett. Thanks for listening!