National Health and Nutrition Examination Survey

2015-2016 Data Documentation, Codebook, and Frequencies

Sex Steroid Hormone - Serum (TST_I)

Data File: TST_I.xpt

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Component Description

This data will allow for population estimates of the selected steriod hormones and related binding protein that can be used to assist in disease diagnosis, treatment, and prevention of disease such as, Polycystic Ovary Syndrome (PCOS), androgen deficiency, cancer, and hormone imbalances in children. An estimated 5 to 7 million women in the United States (U.S) suffer with the effects of PCOS; and PCOS can occur in girls as young as 11 years old. PCOS is the most common hormonal disorder among women of reproductive age and is the leading cause of infertility. Androgen deficiency such as hypogonadism is associated with a range of chronic diseases. The prevalence of symptomatic androgen deficiency in men between 30 and 79 years of age is estimated to be 5.6% (Araujo et al, 2007). Androgen deficiency in men and excess in women and the associated chronic diseases are a public health concern. Estradiol is the key biomarker for assessing reproductive function in females, including amenorrhea, infertility, and menopausal status. Estradiol levels decline greatly with age, and this decrease is associated with increased risk for cardiovascular disease, cognitive impairment, and bone fractures in older populations. Estrogen hormone therapy, or use of estradiol as a supplement, raises health concerns related to estradiol concentration in blood such as elevated levels in postmenopausal women increasing the risk of breast cancer.

Testosterone

Testosterone is the most important adrogenic steroid that has an anabolic effect in humans. It is synthesized in the testes of the male, and in much smaller amounts, in the ovary of the female, and in the adrenal gland of both female and male. In human males, testosterone plays a key role in the development of male reproductive tissues, such as the testis and prostate, as well as promoting secondary sexual characteristics, such as increased muscle and bone mass, and the growth of body hair. The secretion of testosterone is regulated by luteinizing hormone (LH), and is subject to negative feedback via the pituitary and hypothalamus. Most of the circulating testosterone is bound to carrier proteins (sex hormone-binding globulin [SHBG], and albumin). In women, ncreased production of testosterone can cause hirsutism and virilization (depending on the increase). The determination of testosterone in the female is helpful in the evaluation of cengenital adrenal hyperplasia, PCOS, and when an ovarian tumor, adrenal tumor, adrenal hyperplasia, or

ovarian insufficiency is suspected. Testosterone is determined in men when reduced testosterone production is suspected, e.g., in hypogonadism, estrogen therapy, chromosome aberrations (as in the Klinefelter's syndrome) and liver cirrhosis.

Sex hormone-binding globulin (SHBG)

Sex hormone-binding globulin (SHBG) is the blood transport protein for androgens and estrogens. SHBG has a high binding affinity to dihydrotestosterone (DHT), medium affinity to testosterone and estradiol, and only a low affinity to estrone, dehydroepiandrosterone (DHEA), androstendione, and estriol. Albumin, which exists in far higher concentrations than SHBG, also binds sexual steroids – although with a clearly lower binding affinity (e.g. about 100 times lower for testosterone). Its synthesis and secretion are regulated by estrogen (Burger,et al., 2002; Davis, et al. , 2001). SHBG serum concentrations depend on the extent, duration, and the kind of estrogen applied, and how regulation takes place. In the serum, SHBG mainly takes over the transportation of steroids and the reduction/regulation of the effect of androgen (Rosner, et al. 1999; Burger, et al. 2002). Decreased SHBG serum levels are associated with conditions where elevated androgen levels are present or where the effect of androgen on its target organs is excessive. This explains the gender-related differences seen between men and women, especially during puberty.

Measurement of SHBG can be an important indicator of an excessive/chronic androgenic action where androgen levels are normal, but where clinical symptoms would seem to indicate androgen in excess. SHBG is a useful supplementary parameter in the determination of androgen where a relatively high concentration of free androgen (e.g. testosterone) is suspected (Pugeat, et al. 1996).

Elevated SHBG levels can be seen in elderly men, and are often found in patients with hyperthyroidism, cirrhosis of the liver, and some polymorphisms in the SHBG gene (Bhasin, et al 2018). SHBG levels also increase when oral contraceptives, estrogen or antiepileptic drugs are taken. Pregnant women have markedly higher SHBG serum concentrations due to their increased estrogen production.

Decreased SHBG concentrations are often seen with hypothyroidism, polycystic ovarian syndrome (PCOS), obesity, hirsutism, elevated androgen levels, alopecia, acromegaly, and some polymorphisms in the SHBG gene.

Estrogens

Estrogens are responsible for the development of the secondary female sex characteristics. Together with progestogens they control all the important female reproductive processes. The biologically most active estrogen is 17 ß-estradiol. Estrogens are produced primarily in the ovary (follicle, corpus luteum), but small quantities are also formed in the testes and in the adrenal cortex, as well as fat cells. During pregnancy, estrogens are mainly formed in the placenta. About 98% of estradiol is bound to transport proteins (SHBG and albumin). Estrogen secretion has two surges during the menstrual cycle. The determination of estradiol is utilized clinically in the elucidation of fertility disorders in the hypothalamus-pituitary-gonad axis, gynecomastia, estrogen-producing ovarian and testicular tumors and in

hyperplasia of the adrenal cortex. Further clinical indications are the monitoring of fertility therapy and determining the time of ovulation within the framework of in vitro fertilization (IVF).

Eligible Sample

Examined participants aged 6 years and older were eligible.

Description of Laboratory Methodology

Testosterone and estradiol are preformed via isotope dilution liquid chromatography tandem mass spectrometry (ID-LC-MS/MS) method for routine quantitation of serum total testosterone and estradiol based on the National Institute for Standards and Technology's (NIST) reference method. This method was optimized for higher sample throughput and certified by CDC Hormone Standardization Program (HoSt) (Zhou, et al, 2017).

This method employs Liquid-Liquid extraction (LLE) of serum to isolate the steroid. Stable Isotope-labeled testosterone and estradiol are used as an internal standard to correct for sample recovery during the sample preparation process. The method is standardized through CDC's HoSt program.

SHBG is based on the reaction of SHBG with immuno-antibodies and chemo-luminescence measurements of the reaction products that occurs after two incubation periods and subjecting to a magnetic field. The microparticles are captured on an electrode, where a chemiluminescent reaction occurs and can be measured by a photomultiplier tube. The readings are compared to an instrument- and lot-specific calibration curve.

Refer to the Laboratory Method Files section for a detailed description of the laboratory methods used.

There were no changes to the lab method, lab equipment, or lab site for this component in the NHANES 2015-2016 cycle.

Laboratory Method Files

Total Estradiol and Total Testosterone (November 2018)

Sex Hormone-Binding Globulin (November 2018)

Laboratory Quality Assurance and Monitoring

Serum samples are processed, stored, and shipped to the Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA for analysis.

Detailed instructions on specimen collection and processing are discussed in the NHANES Laboratory Procedures Manual (LPM). Vials are stored under appropriate frozen (–30°C) conditions until they are shipped to National Center for Environmental Health for testing.

The NHANES quality assurance and quality control (QA/QC) protocols meet the 1988 Clinical Laboratory Improvement Act mandates. Detailed QA/QC instructions are discussed in the NHANES LPM.

Mobile Examination Centers (MECs)

Laboratory team performance is monitored using several techniques. NCHS and contract consultants use a structured competency assessment evaluation during visits to evaluate both the quality of the laboratory work and the quality-control procedures. Each laboratory staff member is observed for equipment operation, specimen collection and preparation; testing procedures and constructive feedback are given to each staff member. Formal retraining sessions are conducted annually to ensure that required skill levels were maintained.

Analytical Laboratories

NHANES uses several methods to monitor the quality of the analyses performed by the contract laboratories. In the MEC, these methods include performing blind split samples collected during “dry run” sessions. In addition, contract laboratories randomly perform repeat testing on 2% of all specimens.

NCHS developed and distributed a quality control protocol for all the contract laboratories, which outlined the use of Westgard rules (Westgard, et al. 1981) when running NHANES specimens. Progress reports containing any problems encountered during shipping or receipt of specimens, summary statistics for each control pool, QC graphs, instrument calibration, reagents, and any special considerations are submitted to NCHS quarterly. The reports are reviewed for trends or shifts in the data. The laboratories are required to explain any identified areas of concern.

All QC procedures recommended by the manufacturers were followed. Reported results for all assays meet the Division of Environmental Health Laboratory Sciences’ quality control and quality assurance performance criteria for accuracy and precision, similar to the Westgard rules (Caudill, et al. 2008).

Data Processing and Editing

The data were reviewed. Incomplete data or improbable values were sent to the performing laboratory for confirmation.

Analytic Notes

Refer to the 2015-2016 Laboratory Data Overview for general information on NHANES Laboratory Data.

Demographic and Other Related Variables

The analysis of NHANES laboratory data must be conducted using the appropriate survey design and demographic variables. The NHANES 2015-2016 Demographics File contains demographic data, health indicators, and other related information collected during

household interviews as well as the sample design variables. The recommended procedure for variance estimation requires use of stratum and PSU variables (SDMVSTRA and SDMVPSU, respectively) in the demographic data file.

The Fasting Questionnaire File includes auxiliary information such as fasting status, length of fast, and the time of venipuncture.

This laboratory data file can be linked to the other NHANES data files using the unique survey participant identifier (i.e., SEQN).

Detection Limits

The detection limits were constant for all of the analytes in the data set. Two variables are provided for each of these analytes. The variable named ended “LC” (ex., LBDTSTLC) indicates whether the result was below the limit of detection: the value “0” means that the result was at or above the limit of detection, “1” indicates that the result was below the limit of detection. The other variable prefixed LBX (ex., LBXTST) provides the analytic result for that analyteFor analytes with analytic results below the lower limit of detection (ex., LBDTSTLC=1), an imputed fill value was placed in the analyte results field. This value is the lower limit of detection divided by the square root of 2 (LLOD/sqrt[2]).

The lower limit of detection (LLOD) for LBXTST, LBXEST and LBXSHBG are:

Variable Name	SAS Label	LLOD
LBXTST	Testosterone, total (ng/dL)	0.75 ng/mL*
LBXEST	Estradiol (pg/mL)	2.994 pg/mL**
LBXSHBG	SHBG (nmol/L)	0.800 nmol/L

* Multiply by 0.0347 to convert to SI unit nmol/L

** Multiply by 3.67 to convert to SI unit pmol/L

Total testosterone data in the 2015-2016 survey cycle were measured using the same method as in 2013-2014. For analysis involving 2015-2016 testosterone data and data collected prior to the 2013-2014 cycle, please refer to the documentation accompanying the 2013-2014 sex steroid hormone dataset (TST_H) for additional adjustments.

Please refer to the NHANES Analytic Guidelines and the on-line NHANES Tutorial for further details on the use of sample weights and other analytic issues.

References

- Burger H.G., Dudley E.C., Robertson D.M., Dennerstein L. Hormonal changes in the menopause transition. Recent Prog Horm Res. (2002) 57:257-75.
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- Westgard J.O., Barry P.L., Hunt M.R., Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. Clin Chem (1981) 27:493-501.

Codebook and Frequencies

SEQN - Respondent sequence number

Variable Name:	SEQN
SAS Label:	Respondent sequence number
English Text:	Respondent sequence number.
Target:	Both males and females 6 YEARS - 150 YEARS

LBXTST - Testosterone, total (ng/dL)

Variable Name: LBXTST

SAS Label: Testosterone, total (ng/dL)

English Text: Testosterone, total (ng/dL)

Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0.53 to 2000	Range of Values	7207	7207	
.	Missing	814	8021	

LBDTSTLC - Testosterone comment code

Variable Name: LBDTSTLC

SAS Label: Testosterone comment code

English Text: Testosterone comment code

Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	7181	7181	
1	Below lower detection limit	26	7207	
.	Missing	814	8021	

LBXEST - Estradiol (pg/mL)

Variable Name: LBXEST

SAS Label: Estradiol (pg/mL)

English Text: Estradiol (pg/mL)

Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
2.114 to 14000	Range of Values	7150	7150	
.	Missing	871	8021	

LBDESTLC - Estradiol Comment Code

Variable Name: LBDESTLC

SAS Label: Estradiol Comment Code

English Text: Estradiol Comment Code

Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	6060	6060	
1	Below lower detection limit	1090	7150	
.	Missing	871	8021	

LBXSHBG - SHBG (nmol/L)

Variable Name: LBXSHBG

SAS Label: SHBG (nmol/L)

English Text: Sex Hormone Binding Globulin (SHBG, nmol/L)

Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
4.81 to 1031	Range of Values	6959	6959	
.	Missing	1062	8021	

LBDSHGLC - SHBG Comment Code

Variable Name: LBDSHGLC

SAS Label: SHBG Comment Code

English Text: SHBG Comment Code

Target: Both males and females 6 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	6959	6959	
1	Below lower detection limit	0	6959	
.	Missing	1062	8021