MAYO CLINIC LABORATORIES

Test Definition: SHBG1

Sex Hormone-Binding Globulin, Serum

Overview

Useful For

Diagnosis and follow-up of women with symptoms or signs of androgen excess (eg, polycystic ovarian syndrome and idiopathic hirsutism)

An adjunct in monitoring sex-steroid and antiandrogen therapy

An adjunct in the diagnosis of disorders of puberty

An adjunct in the diagnosis and follow-up of anorexia nervosa

An adjunct in the diagnosis of thyrotoxicosis (tissue marker of thyroid hormone excess)

A possible adjunct in diagnosis and follow-up of insulin resistance and cardiovascular and type 2 diabetes risk assessment, particularly in women

Highlights

Sex hormone-binding globulin (SHBG) is a major carrier protein for sex steroids in the blood.

Determination of SHBG concentrations is useful in the investigation of cases of suspected androgen excess such as polycystic ovarian syndrome or idiopathic hirsutism.

SHBG concentration measurements may be useful in the evaluation of infertility, disorders of puberty, thyrotoxicosis, and in the monitoring of sex-steroid and anti-androgen therapies.

Method Name

Immunoenzymatic Assay

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 1 mL

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	90 days	
	Ambient	7 days	

Clinical & Interpretive

Clinical Information

Sex hormone-binding globulin (SHBG), a 95 KDa homodimer, is the blood transport protein for testosterone and estradiol. SHBG is mainly produced in the liver and has a half-life of approximately seven days. SHBG binds reversibly to sex steroids. SHBG has a relatively high binding affinity to dihydrotestosterone (DHT), medium affinity to testosterone and estradiol, and exhibits a low affinity to estrone, dehydroepiandrosterone (DHEA), androstenedione, and estriol. Albumin, which exists at physiologically higher concentrations than SHBG, also binds to sex steroids although with a much lower binding affinity (eg, about 100 times lower for testosterone).

Decreased SHBG serum concentrations are associated with conditions in which elevated androgen concentrations are present or the effect of androgen on its target organs is excessive. Because of the high binding affinity of SHBG to DHT, as compared to estradiol, SHBG has profound effects on the balance between bioavailable androgens and estrogens. Increased SHBG concentrations may be associated with symptoms and signs of hypogonadism in men, while decreased concentrations can result in androgenization in women. SHBG is also regulated by insulin, and a low SHBG concentration often indicates insulin resistance and, consequently, may be a predictor of type 2 diabetes.

Endogenous or exogenous thyroid hormones or estrogens increase SHBG concentrations. In men, there is also an age-related gradual rise, possibly secondary to the mild age-related fall in testosterone production. This process can result in bioavailable testosterone concentrations that are much lower than would be expected based on total testosterone measurements alone.

Reference Values

CHILDREN

Males

Tanner Stages	Mean Age	Reference Interval (nmol/L)
Stage I	10.4	17-135
Stage II	11.1	21-114
Stage III	12.7	12-138
Stage IV	14.5	7.7-67
Stage V	14.2	3.9-40

Females

Tanner Stages	Mean Age	Reference Interval (nmol/L)
Stage I	10.5	16-182
Stage II	10.9	24-121
Stage III	12.5	18-87
Stage IV	14	7.7-108
Stage V	14.9	10-79

ADULTS
Males
> or =18 years: 13.3-89.5 nmol/L
Females
18-46 years: 18.2-135.5 nmol/L
47-91 years, post-menopausal: 16.8-125.2 nmol/L

Interpretation

Many conditions of mild-to-moderate androgen excess in women, particularly polycystic ovarian syndrome, are associated with low sex hormone-binding globulin (SHBG) concentrations. A defect in SHBG production could lead to bioavailable androgen excess, in turn causing insulin resistance that depresses SHBG concentrations further. There are rare cases of *SHBG* variants that follow this pattern. SHBG concentrations are typically very low in these individuals. However, in most patients, SHBG concentrations are mildly depressed or even within the lower part of the reference interval. In these patients, the primary problem may be androgen overproduction, insulin resistance, or both.

Adult SHBG concentrations in adolescent males with signs of precocious puberty support that the condition is testosterone driven, rather than representing premature adrenarche.

Therapies/behavior alterations that potentially increase SHBG concentrations include reducers of bioactivity of androgens (eg, androgen receptor antagonists, alpha-reductase inhibitors) or reduction of insulin resistance (eg, weight loss, metformin, peroxisome proliferator-activated receptor [PPAR] gamma agonists). Clinical assays may not be available for many therapeutic synthetic androgens and estrogens (eg, ethinyl-estradiol). In those instances, increasing SHBG concentrations may be associated with anti-androgen or estrogen therapy, while SHBG reduction can be associated with androgen treatment.

Patients with anorexia nervosa have high SHBG concentrations. With successful treatment, concentrations start to fall as nutritional status improves. Normalization of SHBG precedes, and may be predictive of, future normalization of reproductive function.

Thyrotoxicosis increases SHBG concentrations. In situations when assessment of true functional thyroid status may be difficult (eg, patients receiving amiodarone treatment, individuals with thyroid hormone transport-protein abnormalities, patients with suspected thyroid hormone resistance or suspected inappropriate thyroid-stimulating hormone [TSH] secretion such as a TSH-secreting pituitary adenoma), elevated SHBG concentrations suggests tissue thyrotoxicosis, while a normal level indicates euthyroidism or near-euthyroidism.

SHBG is also produced by placental tissue and therefore values will be elevated during pregnancy. Reference ranges for pregnant females have not been established in our institution.

In patients with known insulin resistance, "metabolic syndrome," or high risk of type 2 diabetes (eg, women with a history of gestational diabetes), low SHBG concentrations may predict progressive insulin resistance, cardiovascular complications, and progression to type 2 diabetes. An increase in SHBG concentrations may indicate successful therapeutic intervention.

A genetic variant of *SHBG* (Asp327>Asn) introduces an additional glycosylation site in 10% to 20% of the population, resulting in significantly slower degradation. These individuals tend to have higher SHBG concentrations for any given level of other factors influencing SHBG.

In laboratories without access to bioavailable testosterone or equilibrium dialysis-based "true" free testosterone assays, sex hormone-binding globulin measurement is crucial in cases when assessment of the free testosterone fraction (free androgen index or calculated free testosterone) is required. At Mayo Clinic Laboratories, both bioavailable testosterone (TTBS / Testosterone, Total and Bioavailable, Serum) and free testosterone (TGRP / Testosterone, Total and Free, Serum) measurements are available. Free testosterone (TGRP) is measured by equilibrium dialysis, obviating the need for sex hormone-binding globulin measurements to calculate free androgen fractions.

Cautions

In rare cases, interference due to extremely high titers of antibodies to analyte-specific reagents (human antimouse or heterophile antibodies) can occur. The laboratory should be alerted if the result does not correlate with the clinical presentation.

For patients presenting with cirrhosis or sub-clinical thyroid conditions, carefully evaluate results as these conditions can potentially cause erroneous sex hormone-binding globulin (SHBG) results.

SHBG results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information.

Clinical Reference

1. Konforte D, Shea JL, Kyriakopoulou L, et al:, Complex biological pattern of fertility hormones in children and adolescents: A study of healthy children from the CALIPER cohort and establishment of pediatric reference interval. Clin Chem. 2013;59(8):1215–1227

2. Pugeat M, Plotton I, de la Perriere, Raverot G, Dechaud H, Raverot V:(Management of endocrine disease hyperandrogenic states in women: Pitfalls in laboratory diagnosis. Eur J Endocrinol. 2018;178(4):141-154

3. Jarecki P, Herman WA, Pawliczak E, Lacka K:Can low SHBG serum concentration be a good early marker of male hypogonadism in metabolic syndrome? Diabetes Metab Syndr Obes. 2019;12:2181-2191.

4. Calzada M, Lopez N, Noguera JA, et al: AMH in combination with SHBG for the diagnosis of polycystic ovary syndrome. J Obstet Gynecol. 2019;39(8):1130-1136

5. Tchernof A, Despres JP: Sex steroid hormone, sex hormone-binding globulin, and obesity in men and women. Horm Metab Res. 2000;32:526-536
6. Kahn SM, Hryb DJ, Nakhle AM, Romas NA, Rosner W: Sex hormone-binding globulin is synthesized in target cells. J Endocrinol. 2002;175:113-120
7. Hammond GL: Access of reproductive steroids to target tissues. Obstet Gynecol Clin North Am. 2002;29:411-423
8. Elmlinger MW, Kuhnel W, Ranke MB: Reference ranges for serum concentrations of lutropin (LH), follitropin (FSH), estradiol (E2), prolactin, progesterone, sex hormone binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEA-S), cortisol and ferritin in neonates, children, and young adults. Clin Chem Lab Med. 2002;40(11):1151-1160

Performance

Method Description

The Access SHBG assay is a sequential 2-step immunoenzymatic (sandwich) assay. Patient sample is added to a reaction vessel along with paramagnetic particles coated with monoclonal anti-sex hormone-binding globulin (SHBG) antibody and saline buffer with proteins. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. A second monoclonal anti-SHBG antibody conjugated to alkaline phosphatase is added to the reaction vessel. After the second incubation in the reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of SHBG in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.(Instruction manual: Access SHBG Sex Hormone-Binding Globulin, A48617. Beckman Coulter, Inc; 04/2020)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 3 days

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.

- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

84270

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SHBG1	Sex Hormone-Binding Globulin, S	13967-5

Result ID	Test Result Name	Result LOINC® Value
SHBG1	Sex Hormone-Binding Globulin, S	13967-5