Sex hormone-binding globulin (SHBG) is a serum glycoprotein exhibiting the unique feature of binding sex steroids with high affinity and specificity. Its serum levels are regulated not only by androgens and estrogens but also by thyroid hormones and other metabolic factors. Several disease conditions are accompanied by altered SHBG levels such as hyper- and hypoandrogenism, thyroid disorders, pituitary diseases, liver disorders, and breast as well as prostate cancer. Additionally, several drugs and alcohol consumption influence serum concentrations of SHBG. In some cases, altered SHBG levels are a specific result of the underlying pathology. In others, they merely constitute an epiphenomenon, which still might offer the possibility of using serum measurements of SHBG as surrogate marker. This review article portrays the different disorders associated with altered SHBG levels and discusses the usefulness of SHBG as disease biomarker from a clinicians as well as from an endocrinological researchers point of view.