Sex hormone binding globulin and testosterone in children and adolescents with type 1 diabetes Mellitus and their siblings

Thesis

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Mohammed Abd El-Monem

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Abstract

Introduction: Type ١diabetes is the most common metabolic disease in childhood.

Aim of the work: is to evaluate the level of sex hormone binding globulin, free and total testosterone levels in type١ diabetes, and to define different factors related to the patients and to the disease affecting their levels.

Subjects and methods: This study was carried out at Diabetes Clinic, Children Hospital; Ain shams University. A total of ٥٦ children and adolescents (٢٠ males and ٣٦ females) with T١DM were enrolled in the study. Thirty eight children and adolescents of their healthy siblings (٢٠ males and ١٨ females) were taken for comparative study. They were matched in age and gender to the study group and had normal blood glucose level.

Total and free testosterone and sex hormone binding globulin levels were measured for both patients and controls.

Results: Diabetic male patients were found to have significantly lower SHBG levels when compared to controls. Male patients had higher levels of total and free testosterone compared to controls, while there was no significant difference between female diabetic patients and controls regarding SHBG, total and free testosterone levels.

Conclusion: This study provides evidence of a relationship between poor glycemic control (confirmed by increased HbA١c) with lower level of SHBG, and higher levels total and free testosterone.

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List of abbreviations

ADA	American Diabetes Association.
BMI	Body mass index.
DHT	Dihydrotestosterone.
DKA	Diabetic ketoacidosis.
DM	Diabetes mellitus.
ELISA	Enzyme linked immunosorbant assay.
GnRH	Gonadotropin-releasing hormone
Hb	Hemoglobin.
HbA1c	glycosylated hemoglobin
HOMA-IR	Homeostasis model assessment-insulin resistance.
HPG	hypothalamic-pituitary-gonadal axis
HREs	Hormone response elements.
HRP	Horseradish peroxidase.
Ht	Height.
IFG	Impaired fasting glucose.
IGF-1	Insulin-like growth factor ١.
LH	Luteinizing Hormone.
MAbs	Monoclonal antibodies.
M/F	Male to female ratio.
PCOS	Polycystic ovarian syndrome.
RBCs	Red blood cells.
SD	Standard deviation.
SDS	Standard deviation score
SHBG	Sex hormone-binding globulin
T	Testosterone
TT	Total testosterone
T1DM	Type ١ diabetes mellitus.
T2DM	Type ٢ diabetes mellitus.
Wt	Weight

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Introduction

Diabetes mellitus is a group of metabolic diseases characterized by high blood glucose levels that result from defects in the body's ability to produce and/or use insulin***(ADA, 2010)***.

Type ١ diabetes is the most common metabolic disease in childhood with an increasing incidence of about ٣ to ٥٪ per year, particularly in preschool children. Despite substantial progresses in diabetes research concerning its pathogenesis and etiology in the last decades, there is no strategy for primary prevention in subjects with subclinical signs of diabetes ***(Kordonouri et al., 2008)***

Insulin down-regulates hepatic production of sex hormone binding globulin (SHBG), which in turn influences sex hormone bioavailability***(Nestler, 1993)***.

Some experts assumed that SHBG is higher in subjects with diabetes; SHBG was related to the absence of endogenous insulin production, irrespective of diabetes type or treatment, and insulin resistance. They found also that testosterone levels

were higher in those with childhood diabetes***(Danielson,*** *٢٠٠٨).*

The effects of childhood-onset diabetes and insulin resistance in nondiabetic individuals on SHBG and testosterone in children and young adults are poorly understood.

Aim of The Work

The aim of our study is to evaluate the level of sex hormone binding globulin, free and total testosterone levels in type١ diabetes, and to define different factors related to the patients and to the disease affecting their levels.

Chapter (1)

Testosterone and sex hormone binding globulin

Testosterone:

Testosterone is a steroid hormone from the androgen group. In mammals, testosterone is primarily secreted in the testes of males and the ovaries of females, although small amounts are also secreted by the adrenal glands. It is the principal male sex hormone and anabolic steroid ***(Corbier et al. 1992)*.**

In men, testosterone plays a key role in health and well-being as well as preventing osteoporosis. On average, an adult human male body produces about forty to sixty times more testosterone than an adult human female body, but females are, from a behavioral perspective (rather than from an anatomical or biological perspective), more sensitive to the hormone. However, the overall ranges for male and female are very wide, such that the ranges actually overlap at the low end and high end respectively ***(Dabbs M and Dabbs JM, 2000)*.**

Physiological effects:

In general, androgens promote protein synthesis and growth of those tissues with androgen receptors. Testosterone effects can be classified as virilizing and anabolic, although the distinction is somewhat artificial, as many of the effects can be considered both. Testosterone is anabolic, meaning it builds up bone and muscle mass.

- Anabolic effects include growth of muscle mass and strength, increased bone density and strength, and stimulation of linear growth and bone maturation ***(Swab and Garcia-Falgueras, 2009).***

- Androgenic effects include maturation of the sex organs, particularly the penis and the formation of the scrotum in the fetus, and after birth (usually at puberty) a deepening of the voice, growth of the beard and axillary hair. Many of these fall into the category of male secondary sex characteristics ***(Swab and Garcia-Falgueras, 2009).***

Testosterone effects can also be classified by the age of usual occurrence. For postnatal effects in both males and females, these are mostly dependent on the levels and duration of circulating free testosterone.