

Pubertal Development and Ovarian Function among Girls with Type 1 Diabetes Mellitus

Thesis

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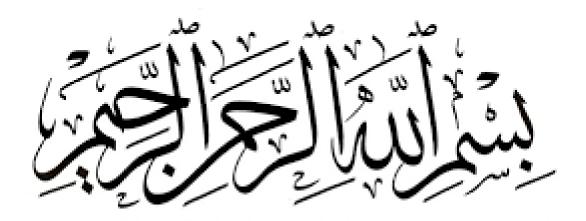
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THIS WORK IS HUMBLY DEDICATED TO MY FAMILY

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Abstract

Background: Despite intensive insulin therapy, some delay in the pubertal development is still observed in girls with type 1 diabetes mellitus (T1DM). In addition, ovarian hyperandrogenism may be observed during late adolescence.

Aim of study: To assess the pubertal development, to detect the presence of hyperandrogenism, and to assess the ovarian function as well as the ovarian morphology in girls with type1diabetes.

Subjects and Methods: Thirteen Egyptian girls with an age range of 13 - 18 years (mean age \pm SD, 15.44 \pm 1.31 yrs) were recruited from Pediatric Diabetes Clinic, Children's Hospital, Ain Shams University, Egypt, for a cross-sectional study. Tanner pubertal staging and age at menarche were evaluated. Anthropometric measurements were assessed. Laboratory investigations were done; HbA1c levels and hormone assays (serum basal and post stimulation levels): FSH, LH, E2, 17OHProg, FTC, Δ 4 androstenedione and DHEAS. Transabdominal ultrasonography was performed. The study findings were compared with normal reference data.

Intervention: GnRH-analogue test with subcutaneous 0.1 mg triptorelin.

Results: The mean age at menarche $(13.24 \pm 1.25 \text{ years})$, among the postmenarcheal T1DM girls, showed no delay, compared to the normal Egyptian girls; seven (53.8%) girls had oligomenorrhea, and 2 (10.5%) girls did not achieve menarche. There was a highly significant delay (P<0.01) in their attainment of sexual maturity (Tanner stage 5). Hirsutism was observed in 1 (7.7%) girl, and none of the girls had acne. Functional ovarian hyperandrogenism (FOH) and biochemical hyperandrogenism were revealed in 1(7.7%) and 2 (15.4%) girls, respectively. According to

the Rotterdam criteria, PCOS phenotypes and PCOM were observed among 4 (30.8%) of the T1DM girls.

Conclusion: Type 1 diabetes could affect pubertal development of the intensively treated girls; where their attainment of sexual maturity, but not their age at menarche, is delayed. Mild manifestations of hyperandrogenism are also observed, indicating ovarian steroidogenic function affection.

Keywords: Type 1 diabetes mellitus - Insulin - Metabolic control - Puberty - Menarche - functional ovarian hyperandrogenism (FOH)

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ABBREVIATIONS

< : Less than.

≤ Less than, or equal to.

> : Greater than.

≥ : Greater than, or equal to.

 χ^2 test : Pearson Chi-Square test

17OHProg: 17-hydroxyprogesterone

ACTH: Adrenocorticotropic hormone

ADA : American Diabetes Association

AE-PCOS: Androgen Excess and PCOS (Society)

BMI : Body mass index

(B) : Tanner Breast stage

CGM : Continuous Glucose Monitoring

CSII : Continuous subcutaneous insulin infusion

DCCT: The Diabetes Control and Complications Trial

DHEA: Dehydroepiandrosterone

DHEAS: Dehydroepiandrosterone sulfate

DNA : Deoxyribonucleic acid

DSME: Diabetes self-management education

DSMS: Diabetes self-management education and support

EDTA : Ethylenediaminetetraacetic acid

ESHRE/ASRM: The European Society for Human Reproduction and

Embryology and the American Society for

Reproductive Medicine

FAI: Free androgen index

FF: Ovarian (follicular fluid)

FG score : Ferriman-Gallwey score

FOH : Functional ovarian hyperandrogenism

FPG: Fasting plasma glucose

FSH: Follicle-stimulating hormone

FT : Free Testosterone

FTC : Calculated Free Testosterone

GAD: Glutamic acid decarboxylase 65 autoantibodies

GH: Growth hormone

GLP-1 : Glucagon-like peptide 1 (GLP-1) receptor agonists or GLP-1

analogues

GLUTs: glucose transporter proteins

GnRH: Gonadotropin-releasing hormone

HbA1/ HbA1c/A1c: Glycated Hemoglobin (hemoglobin A1c)

HGH: Human growth hormone.

HLA : Human leukocyte antigen.

HPO: Hypothalamic-pituitary-ovarian

HPG: Hypothalamic-pituitary-gonadal

IA2 : Tyrosine phosphatase-like insulinoma antigen 2

IAA : Insulin autoantibodies

ICA512 : Islet cell antibody 512

IFCC: International Federation of Clinical Chemistry

IFG: Impaired fasting glucose

IGF- I: Insulin-like growth factor I

IGF- II: Insulin-like growth factor II

IGFBP-3: Insulin-like growth factor-binding protein 3

IGT: Impaired glucose tolerance

ISPAD: The International Society for Pediatric and Adolescent

Diabetes

IV : Intravenous

IVGTT: Intravenous glucose tolerance test

LH: Luteinizing hormone

LHRH: LH-releasing hormone

LOV: Left ovarian volume

MDI : Multiple Daily Injections

MRI scans : Magnetic resonance imaging

NA : Not applicable

NEFAs: Non-esterified fatty acids

NICHD criteria: The National Institute of Child Health and Human

Development

NIP : Nutritional Intervention to Prevent

NPH-insulin: Neutral Protamine Hagedorn *or* Isophan (Intermediate

acting) insulins

OGTT: Oral glucose tolerance test

(PH) : Tanner Pubic Hair stage

P value : Probability value

PCOM: Polycystic ovarian morphology

PCOS: Polycystic ovary syndrome

RIA : Radioimmunoassay

ROV: Right ovarian volume

r : Correlation coefficient

sc : Subcutaneous

SD : Standard deviation

SDS: Standard deviation score (z-score)