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

Thesis

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بسم الله الرحمن الرحيم

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 ± SD, 15.44 ±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, Δ4 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 ±1.25 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)