Prevalence of polycystic ovary syndrome and its clinical profile in young females with type 1 diabetes mellitus
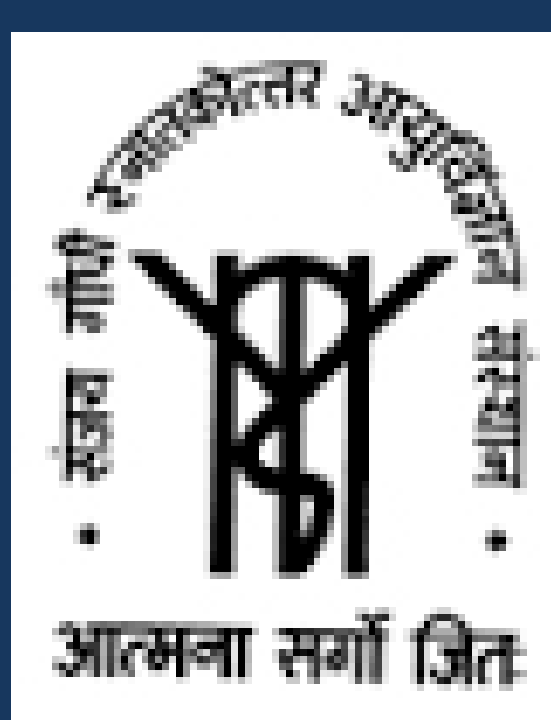
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Introduction

Menstrual irregularities and reproductive abnormalities are known in women with type 1 diabetes (T1DM). These are not only related to metabolic control but are also due to hyperandrgenism (HA). This HA is due to a) hyperinsulinemia due to systemic administration of supraphysiologic doses of insulin for good glycemic control and b) insulin resistance due to glucotoxicity and abnormal gain of fat mass during puberty. Coexistence of type 1 diabetes, HA and polycystic ovary syndrome can increase the risk of micro and macrovascular complications many folds in these young women

Aim

To assess prevalence of polycystic ovary syndrome and its clinical profile in young women with type 1 diabetes

Methods

Sixty five young women with type 1 diabetes were enrolled from 1st October 2014 to 1 December 2015. During their follicular phase they underwent detailed history, examination, hormonal evaluation and transabdominal ultrasound (performed by a single observer). Diagnosis of PCOS was based on Rotterdam criteria. T1DM women with PCOS were compared with age and BMI matched PCOS women without diabetes taken from a cohort attending our endocrine clinic.

Results

Table – 1: Baseline characteristics of patients

Parameter	T1DM (n=65)	No PCOS (n=47)	PCOS (n=18)	p value*
Age in years	20 (11-40)	12-40 (22)	11-31 (19)	.45
Age of onset of DM	12 (3-31)	3-31 (13)	3-27 (12)	.84
Age of menarche	13 (10-18)	10-18(13)	10-17 (13)	.65
Duration of DM in years	6 (1-27)	1-27 (6)	1-22 (5)	.2
Daily insulin dose (U/ kg)	1.08 (.38-2.54)	.38-2.33(1.08)	.7-2.54 (1.05)	.84
BMI (kg/m^2)	20.83 (14.86-29.69)	16.89-27.3 (20.4)	14.8-29.6 (21.5)	.36
Waist to hip ratio	.91 (.79-1.11)	.79-1.1 (.91)	.84-1.02 (.91)	.69
Mean HbA1c (%)	7.2 (5.45-11.06)	5.45-11.06 (7.2)	5.65-9.86 (6.9)	.96
Maximum size of ovary	9.79 (3.64-23.65)	3.64-23.65 (8.4)	7-18.2 (12.1)	0.001
Maximum no. of follicles	7.5 (1-16)	1-14 (6)	1-16 (12.5)	0.0002
Testosterone (nmol/l)	1.1 (.02 – 6.37)	.02 – 1.86 (1.06)	.48 – 6.37 (1.8)	0.0001
DHEAS (μmol/l)	4.54 (.06 – 14.07)	.06 – 10.7 (4.05)	1.33 – 14.07 (5.7)	0.001
SHBG (nmol/l)	63.2 (20 – 144)	28.9 – 144 (65.6)	20 – 101 (54.4)	0.29
Free androgen index	1.96 (.02 – 11.01)	.02 – 4.46 (1.66)	.83 – 11.0 (3.12)	0.0005

Table – 2: Comparison of characteristics between subjects who have PCOS based on the onset of diabetes

Parameter	Pre pubertal (n=10)	Post pubertal (n=8)	p value
Age (yrs)	19 (11-25)	19 (16-31)	.59
Age of onset of DM (yrs)	9.5(3-13)	17 (11-27)	
Age of menarche (yrs)	14 (10-17)	13 (10-14)	.053
Duration of DM in years	7 (1-22)	3.5 (1-6)	.097
BMI (kg/m^2)	22.4 (14.8-26.7)	20.9 (17.4-29.6)	.47
Waist to hip ratio	.93 (.86-1.02)	.91 (.84-1)	.72
Daily insulin dose U/kg	.81 (.7-1.4)	1.2 (.85-2.54)	.65
Mean HbA1c %	7.55 (6.35 – 9.3)	6.75 (5.65-9.86)	.423
Maximum size of ovary	13.0 (8.6-16.3)	11.3 (7-18.2)	.51
Maximum number of follicles	13.5 (1-16)	12 (7-15)	.82
Testosterone (nmol/l)	1.76 (.48– 2.95)	1.94 (1.94– 6.37)	.32
DHEAS (μmol/l)	5.27 (2.63-14.07)	6.62 (2.45-11.21)	.88
SHBG (nmol/l)	57.9 (20-90.6)	55.05 (22.7-101)	1.0
Free androgen index	3.06 (.83-5.13)	2.45 (1.19-3.82)	.54

All data expressed in median (range).

Table – 3: Comparison of PCOS cases among T1DM patients with age and BMI matched PCOS controls

Parameter	PCOS N=18	Controls N=18	p value
Age (yrs)	11-31 (19)	17-28 (20)	0.25
Age of menarche	10-17 (13)	14 (12-16)	0.56
BMI (kg/m^2)	21.5 (14.8-29.6)	22.55 (16.2-29.3)	0.55
Waist to hip ratio	.84-1.02 (.91)	.86 (.68 – 1.02) or .85 ± .08	.004 (with t test also)
Modified FG score	1.5 (0 – 17)	11.5 (0 – 21)	0.04
Testosterone (nmol/l)	1.8 (.48 – 6.37)	1.37 (.18-3.9)	.12
DHEAS (μmol/l)	5.7 (1.33 – 14.07)	5.5 (1.76-11.53)	.44
SHBG (nmol/l)	54.4 (20 – 101)	28.3 (13.9-153)	.004
Free androgen index	3.12 (.83 – 11.0)	4.88 (.99-18.8)	.58

- Both the androgens—testosterone and DHEAS *(r = 0.51, P < 0.001)* correlated with each other
- SHBG showed a negative correlation with BMI *(r = -0.31, P = .01)*
- Serum testosterone levels *(r = .32, P = .01) was* positively correlated with the maximum recorded ovarian volume of either of the ovaries
- Serum levels of DHEAS correlated with the mean daily dose of insulin *(r=.26, P = .04)*
- The mean HbA1c levels did not correlate with the mean duration of menstrual cycles within the whole population

Review of literature

	Number of subjects	Hirsutism by mod FG>8	Hyperandr-ogenemia	PCOS by NIH	PCOS by Rotterdam criteria	AES criteria
Escobar-Morreale et al.	85	30.6%		18.8%		
Codner et al.	42	28.6%	50%	11.9%	40.5%	
Zachurzok et al.	47	6.4%	36.7%		19.2%	
Amato et al.	103					36.89%
Dabadghao (present study)	65	3.1%	26%	10%	27%	21%

- Escobar-Morreale HF et al. High prevalence of the polycystic ovary syndrome and hirsutism in women with type 1 diabetes mellitus. JCEM, 2000 Nov;85(11):4182-7.
- Codner E, et al. Diagnostic criteria for polycystic ovary syndrome and ovarian morphology in women with type 1 diabetes mellitus. JCEM, 2006 Jun;91(6):2250-6.
- Amato MC et al. No phenotypic differences for polycystic ovary syndrome (PCOS) between women with and without type 1 diabetes mellitus. JCEM 2014 Jan;99(1):203-11.

Discussion

- Studies with larger number of patients followed right from the onset of diabetes required to study the natural history of hyperandrogenism.
- Follow up is required to see if treatment of hyperandrogenism has any impact on the development and course of complications of diabetes.

Conclusion

- High prevalence of PCOS and associated menstrual irregularities in patients with type 1 diabetes.
- Clinical features of hyperandrogenism are less common so the diagnosis of PCOS may be missed and should be actively sought.
- Prevalence is not related to metabolic control , age of onset of diabetes and the daily insulin dose.

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Diabetes

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