Evaluation of The Gonadotrophin Levels (LH & FSH) in The Sera of Some Iraqi Female Patients with DM1

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Abstract

This study has focused on gonadotrophins (luteinizing hormone and follicle stimulating hormone) in the sera of (61) Iraqi female patients with type 1 diabetes mellitus with duration of the diseases equal to 8.26±7.7 year. In addition to control group involving (35) healthy women.

We found delay in menarche about 1 year in the patients with DM1 when compared with the control group, and the family history to type 1 diabetes mellitus is present in (36.1%) of the diabetic subjects,and a highly significant increase was found in HbA_{1c} range; (75.4%) of patients had $HbA_{1c} > 8$.

By using Enzyme Linked Immunosorbent Assay (ELISA) technique; LH and FSH levels in the patient groups there were highly significant differences ($P<0.01$) when compared with the control group, so the distribution of each hormone was divided into three levels (normal, high, and low), and Patients were divided according to their menstrual frequency (normal cycle, oligoamenorrhea, and secondary amenorrhea), highly significant differences ($P<0.01$) were present between the levels; and between the mean concentrations of (LH and FSH) in these groups.

Elevated HbA_{1c} range had no relation with (LH & FSH) levels, but it might be associated with it. And no significant relation ($P>0.05$) was found between mean BMI and the hormonal levels (LH & FSH), menstrual frequency, and HbA_{1c} ranges.

(**Abbreviations: BMI,** Body mass index; **ELASA,** Enzyme Linked Immunoabsorbent Assay; **FSH,** Follicle Stimulating Hormone ; **GnRH,** Gonadotophin Releasing Hormone; **HbA_{1c}** , Hemoglobin A_{1c} ; **LH,** Luteinizing Hormone**;** **PCOS,** Polycystic Ovary Syndrome**; T1DM,** Type 1 Diabetes Mellitus **)**

الخلاصة

تناول البحث دراسة مستويات الهورمونات المحفزه للمناسل (الهرمون اللوتيني LH و هرمون محفز الجريبات FSH) في عيناتِ لأمص ال **(61)** إمرأة عراقي ة مصابه بداء السكري من النوع الأول تراوحت فترة اصابتهن بالمرض **8.26±7.7** سَنَة، بالأضافة إلى مجموعة السيطره التيَ تضمّن ت **(35)** امرأة سليمة.

من مراقبة الدوره الشهريه للنساء المصابات بداء السكري من النوع الأول لوحظ تأخر سن البلوغ حوالي سنه واحده مقارنة" ببلوغ مجموعة السيطره، وأن(36.1%) من النساء المصابات لديهن حاله مماثله في العائله(قرابه من الدرجه الاولى) للأصابه بمرض السكري من النوع الاول. وقد تم قياس مستوى الهيموغلوبين من نوع A_{1c} في الدم ووجد زياده معنويه واضحه بين مستوياته حيث ان (75.4%) من المصابات لديهن A_{1c}>8.

تم قياس مستوى (FSH & LH) بتقنية (ELISA)؛ ووجد إختلافَ معنوي كبير (P<0.01) عند المصابات مقارنه بمجموعة السيطره،وعليه تم تصنيف كل هورمون الى ثلاث مستويات (طبيعي، عالي، وواطئ). ثم صنفت المصابات بالأعتماد على انتظامية الدوره الشهريه (دوره منتظمه، قليلة ال حدوث ، وانقطاع الطمث الثانوي)، ووجد اختلاف معنوي كبير (P<0.01) بين مستويات وتراكيز (LH & FSH) في هذه المجاميع.

لوحظ عدم وجود علاقه ترابطيه بين ارتفاع مستوى HbA_{1c} وارتفاع مستويات (LH & FSH)، لكنه قد يترافق ارتفاعهما سوية"، كما انه لاتوجد علاقه معنويه (P>0.05) بين معامل كتلة الجسم (B.M.I) وبين كلا من مستويات (FSH&LH)، انتظامية الدوره الشهريه، ومستويات HbA_{1c}.

Introduction

(LH & FSH) are glycoprotein hormones releasing from the anterior pituitary gland, having similar α subunits that contain 89 amino acid residues, while β subunits of LH and FSH are different as well as their molecular weight (28 KD and 33 KD respectively)[1][2][3]. The secretion of both LH and FSH is stimulated by gonadotrophin releasing hormone (GnRH) from the hypothalamus and both hormones are subjected to feed back loops regulation by the ovarian hormones (short feed back on the pituitary)[4].

High levels of ovarian hormones decrease the release of LH and FSH (negative feed back) while low levels of ovarian hormones promote the secretion of LH and FSH (positive feed back)[5].

The clinical significance of LH&FSH is to aid in the diagnosis of pituitary disorders, premature ovarian failure, menstrual irregularities (such as: amenorrhea, oligoamenorrhea…), and polycystic ovary syndrome (PCOS)[6][7].

Recently an increased prevalence of PCOS has been observed in adult women with Type (1) diabetes mellitus (DM1)[8][9]. It is possible that the metabolic milieu of Type (1) diabetes is associated with a defect in peripheral glucose disposal, specifically due to reduced glucose transport in skeletal muscle. Reduction in insulin binding, and inhibition of binding by insulin antibodies, seems not to play a part. Elevated hepatic glucose output due to impaired hepatic insulin sensitivity may be present in poorly controlled patients and contribute to insulin resistance and menstrual abnormalities[10][11].

Menstrual abnormalities, especially irregular cycles, are common in diabetic women, particularly in those with obesity and poor diabetic control. Many women with type 1 diabetes have anovulatory cycles, with oligo or secondary amenorrhea although oligomenorrhea is more common among diabetic women than general population [12][13][14].

Materials and Methods

Sixty one females with type 1 diabetes mellitus on insulin therapy were selected from people attended to the specialized center for endocrinology and diabetes (Al- Kindey hospital) during the period from November 2005 to May 2006, with duration of the diseases equal to 8.26±7.7 year, and their ages ranged from 14-37 years.

A careful history was obtained from patients including age, duration of DM, family history of type 1 diabetes mellitus, marital status, menstrual history including (age of menarche, duration of cycle, and duration of menstrual disturbances, if any, associated with the symptoms of infertility or abortions), weight and height, and all patients were free from medications affecting hormones levels.

Evaluation of each patient is done by detecting the body mass index (BMI of 18.5–24.9 indicates a person of normal weight, a person with a BMI of 25–29.9 is overweight, and a person with a BMI of ≥ 30 is obese), hemoglobin A_{1c} blood test has been measured by using the Variant Hemoglobin A_{1c} program developed by BIO-Rad, and serum gonadotrophins hormones levels (LH & FSH) by using ELASA test (Biocheck kits , Inc. (U.S.A)), excluding pregnancies and excluding the test during the days (12-16) from the cycle period to avoid the mid cycle maximum and to standardize the result.

As a control, thirty five normal females with a normal regular menstrual cycle and a normal body mass index, their ages ranged from 14-39 years, were included in this study. They were not complaining from any endocrine disorder or using drugs.

Blood samples (8-10 ml) were collected from each patient by vein puncture,(1 ml) of the whole blood was put in EDTA tube, mixed gently and used for hemoglobin A_{1C} test and the rest was centrifuged at 3000 r.p.m for 10 min after allowing the blood to clot at room temperature. The sera were aliquoted and frozen at -20 ^{o}C until the assay day.

Results & Discussions

1. The age range of patients and control group

Patients and control groups are classified in table (1) below according to their age range.

Table (1) Distribution of patients & controls according to Age range (Year).

Age range (Year) patients	N	%	Age range (Year) controls	N	%	Comparison of significance by Kruskal-Wallis Test
14-19	17	27.9	14-19	6	23.1	(P<0.01)
20-29	38	62.3	20-29	21	60	
30-37	6	9.8	30-39	8	16.6	
Total	61	100	Total	35	100	

This table showed that the majority of patients were in the reproductive age between (20-29) years and teenage patients from (14-19) years. Moreover it was clear that patients in the late reproductive age between (30-37) years were the least. The analysis of data showed highly significant differences (P< 0.01) between the percentages of patients in the age group (20-29) years when compared with the other age groups, the controls groups were matched for age with the diabetic patients to avoid any influence of age on the results. Zargar et. al., showed in study revealed DM1 as the commonest form of DM seen in the age group of < 40 years [15]. Yeshaya et. al., examined the cycle length irregularities in young women with type 1 DM (mean age 22) nearly the mean age used in this study (23 year) [16]. Adcock et. al., reported the menstrual irregularities are more common in adolescents with type 1 diabetic with poor glycaemic control [12], and some studies linked women with DM1 (mean age 23.4) with polycystic ovaries [17].

2. The family history

The data demonstrated by table (2) show a significant difference (P< 0.05) between the percentage of the family history to DM1 (first degree relative).

Table (2) Distribution of patients according to Family history.

Family history	N	%	Comparison of significance by Binomial test
Positive	22	36.1	(P<0.05)
Negative	39	63.9	
Total	61	100	

According to researches a strong family history of DM is seen more frequently with type 2 rather than type 1 [15], O'Leary et. al., found that familial' cases represent about 10% of type 1 diabetes while about 27% in type 2 [18].

3. The menarche

The mean age at menarche was higher in type 1 diabetic women compared with the control group in table (3). This result is similar to those reported by American Diabetes Association (2005).

Table (3) Mean distribution of age (Year) & menarche age (Year) in studied group.

Studied group	Age (Year)		Menarche age (Year)	
	Mean±SD	(Sig.)	Mean±SD	(Sig.)
Healthy Control	25.43±6.55	-	11.17±0.82	-
Patients (DM1)	22.85±5.86	(P>0.05)	12.77±0.79	(P>0.05)

Bergquist; Kjaer et. al.; Cawood et. al.; Dorman et. al.; and Danielson have also reported delay 1 year in menarche type 1 diabetes women as well as a later menarche among those with

an earlier age at onset of DM [14] [19] [20] [21] [22]. In contrast to the finding of Schriock et. al., who revealed that menarche occurs earlier or at the same time as in controls if diabetes occurs prior to the onset of puberty [23].

Griffin et. al., stated that diabetes onset before puberty may disrupt the hypothalamic-pituitary- gonadal axis and may delay ovarian maturation and sex hormone production and/or cause weight loss, decreasing body fat important for menarche to occur [24].

4. Luteinizing and follicle stimulating hormone levels in patients and healthy control group

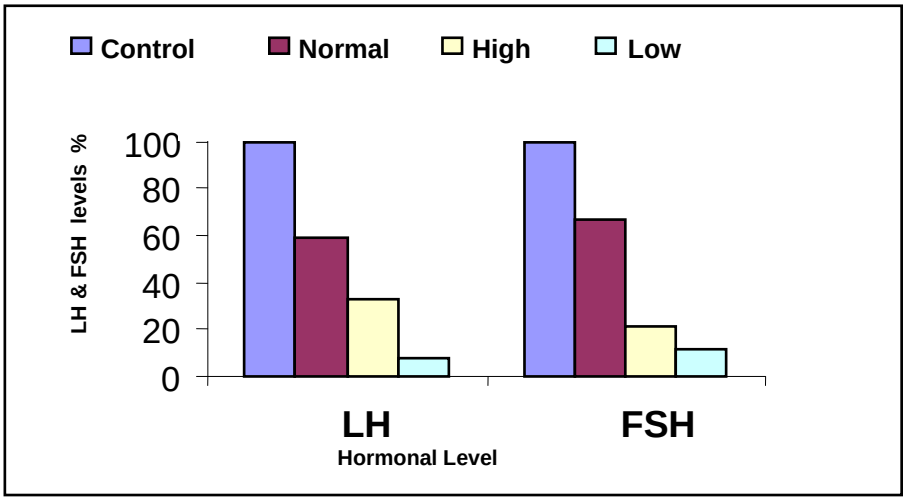
Table and figure (4) showed the mean distribution of the glycoprotein hormones concentrations (LH & FSH) to the females patients with type 1 diabetes mellitus in three different hormonal levels with the minimum & maximum value to each hormonal level when compared with the mean concentration of the normal controls, a highly significant difference ($P<0.01$) was observed between normal, high and low hormonal levels groups for LH & FSH consequently.

The majority of patients have normal hormonal levels with a percentage 59% to LH and 67.2% to FSH when compared with the healthy controls. The result agrees partly with [Djursing et. al.; and Ghazi] [13] [25] the different result could reflect variation in the selection of patients and/or the different lifestyle factors (e.g., physical activity, nutrition, education, and socioeconomic status). The high hormonal levels of LH and FSH were found in 32.8% and 21.3% of the patients consecutively, while the low hormonal levels were found in 8.2% to LH and 11.5% to FSH. Some authors have reported altered pituitary secretion of luteinizing hormone [26] and reduced response of LH to GnRH [27] in type 1 diabetic patients while others reported a normal [28] or enhanced LH response [29]. There was no study specialized of LH and FSH in Iraqi female patients with type 1 diabetes mellitus. So this is the first study in this field compensation of the different hormonal levels.

Table & figure (4) Mean distribution of (LH & FSH) in difference hormonal levels to the patients & healthy controls.

Hormonal levels IU/l		N	%	Mean	Std. Deviation	Std. Error	Min.	Max.	ANOVA (f-test) P-value
LH IU/l	Healthy controls	35	100	9.372	4.936	0.834	1.40	17.9	(P<0.01)
LH IU/l	Normal	36	59	9.615	4.039	0.673	4.00	17.20	
	High	20	32.8	31.381	3.053	0.670	18.60	60.0	
	Low	5	8.2	0.716	0.220	0.098	0.50	1.0	
	Total	61	100						
FSH IU/l	Healthy controls	35	100	6.328	3.725	0.629	1.20	14	(P<0.01)
FSH IU/l	Normal	41	67.2	7.560	3.483	0.544	1.60	14.00	
	High	13	21.3	21.061	9.194	2.550	14.30	40.10	
	Low	7	11.5	0.471	0.149	0.056	0.20	0.70	
	Total	61	100						

Hormonal levels		LSD (F-test) Sig.	
		LH	FSH
Normal(DM1)	High	(P<0.01)	(P<0.01)
	Low	(P>0.05)	(P<0.01)
High	Low	(P<0.01)	(P<0.01)



5. LH & FSH concentration in the Studied groups dividing them according to the menstrual frequency

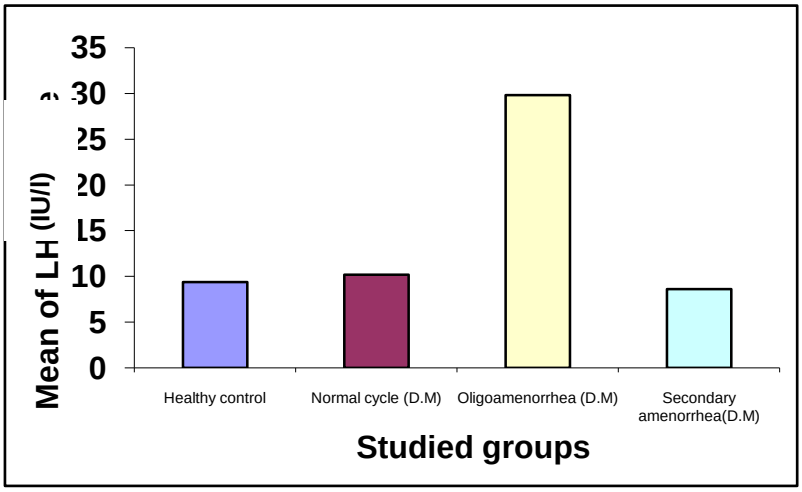
Yeshaya et. al.; Dorman et. al.; and (Arrais & Dib) reported that young women with type 1 diabetes have a delayed age at menarche and are at higher risk for having menstrual irregularities than nondiabetic women of a similar age [16] [21] [30]. Kjaer et. al., found that >30% of the women with type 1 diabetes report problems, such as amenorrhea, polymenorrhea, and oligomenorrhea throughout their reproductive years [19]. The data illustrated by table and figure (5a) clearly shows a highly significant difference ($P<0.01$) between the mean concentration of LH in oligoammenorrhea group which have a higher percentage (41%) than the other groups. On the other hand (LSD) F- test shows a highly significant difference to LH mean concentration in oligoamenorrhea groups in detail. The data agree with Virdis et. al., and Schroeder et. al., who suggested that menstrual abnormalities consisted of oligomenorrhea rather than increased bleeding frequency present in diabetic adolescents [31] [32]. Increased LH levels in this group may be due to polycystic ovarian syndrome, in which menstrual disturbance (amenorrhea, oligoamenorrhea, polyamenorrhea…etc.) are major symptoms [33]. Conder et. al., found that 40.5% of women with DM1 had PCOS [17], and Escobar-Morreale et al, reported a prevalence of 18.8% for PCOS in women with DM1 [8].

Roldan et. al., found that hyperanderogenism (which is an important characteristic symptom of PCOS) comes mostly from androgen synthesis by the ovaries [34], and this androgen will be converted to estrogen which could facilitate secretion an increased amount of LH leads to an increased ovarian androgen production and impaired follicular maturation and anovulation leading to antral follicles and increasing the ovarian volume [35]. An increased secretion of LH could also result from inappropriate secretion of hypothalamic GnRH. (central nervous system abnormalities) because hypothalamic-pitutary-ovary axis may be distributed in type 1 diabetes [24] [36].

Table & figure (5a) Mean distribution of (LH) concentration in the studied groups (dividing them according to the menstrual frequency).

Studied groups	N	%	Mean (LH) IU/l	Std. Deviation	Std. Error	Mini. IU/l	Maxi. IU/l	ANOVA (f-test) P-value
Healthy control	35	100	9.372	4.936	0.834	1.40	17.9	(P<0.01)
Normal cycle (DM1)	24	39.3	10.179	4.181	0.853	4.50	18.6	
Oligoamenorrhea(DM1)	25	41	25.198	16.230	3.268	0.50	60.6	
Secondary amenorrhea(DM1)	12	19.7	8.590	8.307	2.398	0.57	28.5	
Total	61	100						

Studied groups		LSD (F-test) Sig.
Healthy control	Normal cycle (T1DM)	(P>0.05)
	Oligoamenorrhea (T1DM)	(P<0.01)
	Secondary amenorrhea (T1DM)	(P>0.05)
Normal cycle (DM1)	Oligoamenorrhea (T1DM)	(P<0.01)
	Secondary amenorrhea(T1DM)	(P>0.05)
Oligoamenorrhea (DM1)	Secondary amenorrhea(T1DM)	(P<0.01)



In the same figure and table, the analyses of data in (LSD) F-test show no significant difference (P>0.05) between the mean LH concentration in secondary amenorrhea group with healthy control group and normal cycle DM1 group consecutively. In the secondary amenorrhea

group we observe a lower mean to LH plasma concentration than the other groups, the result observed agrees with Griffin et. al.; La Marco et. al.; and Strotmeyer et. al., who suggested that the hypothalamic gonadotrophin releasing hormone pulse generator slows, decreases luteinizing and follicle stimulating hormone stimulation causing menstrual dysfunction in these women [24] [37] [38].

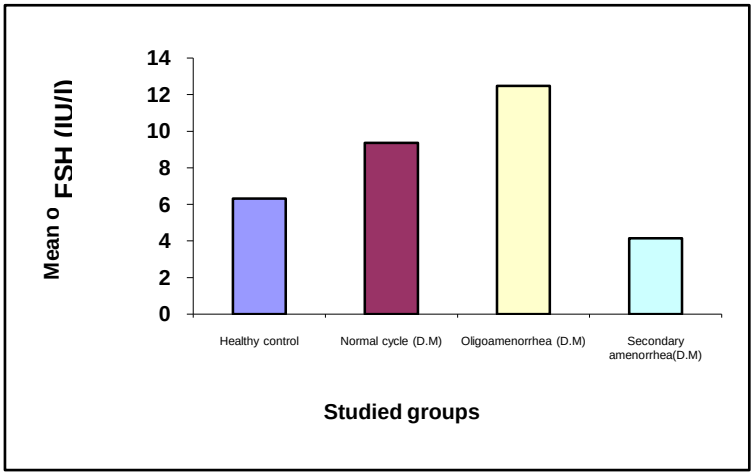
The results in table and figure (5b) show that there are a highly significant difference ($p<0.01$) between the mean concentration (IU/l) of FSH in the groups illustrated above as seen in LH mean concentration in table and figure (5a). The oligoamenorrhea group has the elevated value of FSH mean concentration than the other groups but lesser value than LH in the some group (oligoamenorrhea group) with ratio LH/FSH approximately 2:1. An increased secretion of FSH could result from inappropriate secretion of hypothalamic GnRH. (central nervous system abnormalities) [36].

The secondary amenorrhea group shown in the same table and figure has the lowest value of mean FSH concentration, the result agrees with Griffin et. al.; La Marco et. al.; and Strotmeyer et. al., who found that the secondary amenorrhoic women with insulin dependent diabetes have a lower plasma concentration of FSH than the diabetic normal cycle and controls [24] [36] [37]. In those women there may be a decrease in hypothalamic drive or a decrease in count/ quality of oocytes due to an increased rate of atresia, possibly through the effects of insulin deficiency. The (GnRH) pulse generator slows down and this decreases luteinizing and follicle stimulating hormone stimulation and, in particular, this may occur in women with poor diabetic control [29].

Table & figure (5b) Mean distribution of (FSH) concentration in the studied groups (dividing them according to the menstrual frequency).

Studied groups	N	%	Mean (FSH) IU/l	Std. Deviation	Std. Error	Mini. IU/l	Maxi. IU/l	ANOVA (f-test) P-value
Healthy control	35	100	6.328	3.725	0.629	1.40	14.00	(P<0.01)
Normal cycle(DM1)	24	39.3	9.370	4.080	0.832	0.50	15.70	
Oligoamenorrhea(DM1)	25	41	12.492	10.938	2.187	0.20	40.10	
Secondary amenorrhea(DM1)	12	19.7	4.155	3.581	1.034	0.40	10.90	
Total	96	100						

Studied groups		LSD (F-test) Sig.
Healthy control	Normal cycle (DM1)	(P>0.05)
	Oligoamenorrhea (DM1)	(P<0.01)
	Secondary amenorrhea (DM1)	(P>0.05)
Normal cycle (DM1)	Oligoamenorrhea (DM1)	(P>0.05)
	Secondary amenorrhea (DM1)	(P<0.05)
Oligoamenorrhea (DM1)	Secondary amenorrhea (DM1)	(P<0.01)



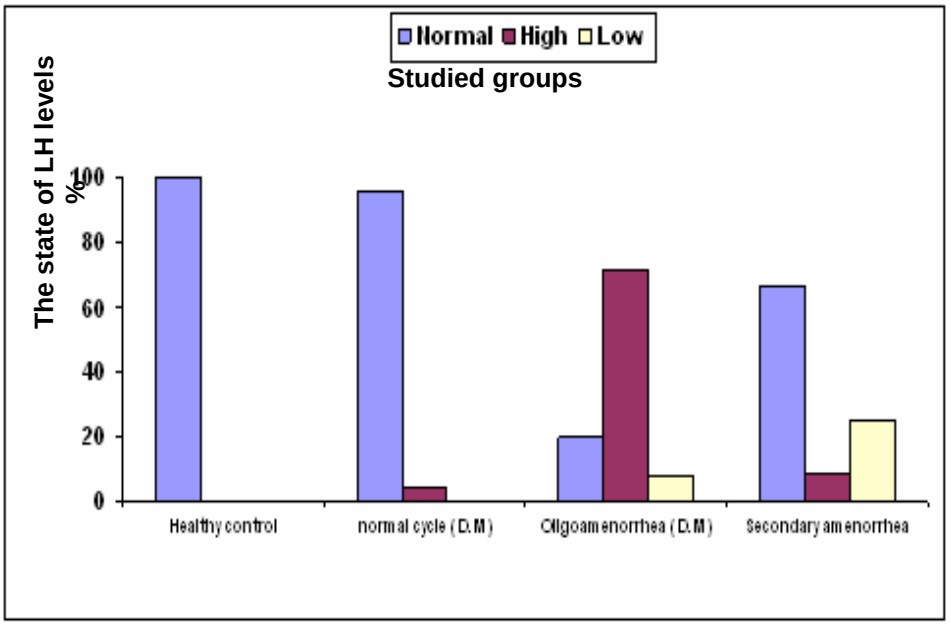
6. LH & FSH levels in the studied groups dividing them according to the menstrual frequency

From table and figure (6a, b) below, all the details of LH and FSH levels in each group have been shown; normal LH level has been presented with a percentage (56 %) in the studied groups including cases with menstrual disturbance (oligoamenorrhea and secondary amenorrhea), as well, in FSH levels in table and figure (6b) ; normal FSH level is present in (67.2 %) of the whole groups, which agree with [Djursing et. al.; and Ghazi S.] [13] [25]. In the menstrual disturbance groups, we can notice normal levels of gonadotrophins LH and FSH. The result agrees with those observed by Djursing et. al., who suggested that anovulating T1DM patients have a normal gonadotrophins LH and FSH like regularly menstruating diabetic type 1 patients [13]. In the secondary amenorrhea groups; the normal LH and FSH levels are present in (66.7 %), whereas in oligoamenorrhea groups; the normal LH levels are (20 %) and FSH were (56 %). Grossman et. al., have found a normal LH and FSH response to GnRH stimulation in well glycemic control [28], and Felig have suggested that the whole abnormality of gonadotropic function may be related to disturbances in carbohydrate homeostasis [39]. Elevated luteinizing and follicle stimulating hormone levels have been (72 %) and (36 %) in oligoamenorhea group consecutively, excess steroidogenesis in DM1 and the abnormalities of insulin like growth factor-1 (it's receptors are on the ovary in addition to insulin receptors) affect on steroidogenesis and may play a role in LH and FSH disturbance [17].

Table & figure (6a) The state of LH levels in the groups under study.

Studied groups		LH level			Total
		Normal	High	Low	
Healthy control	N	35	0	0	35

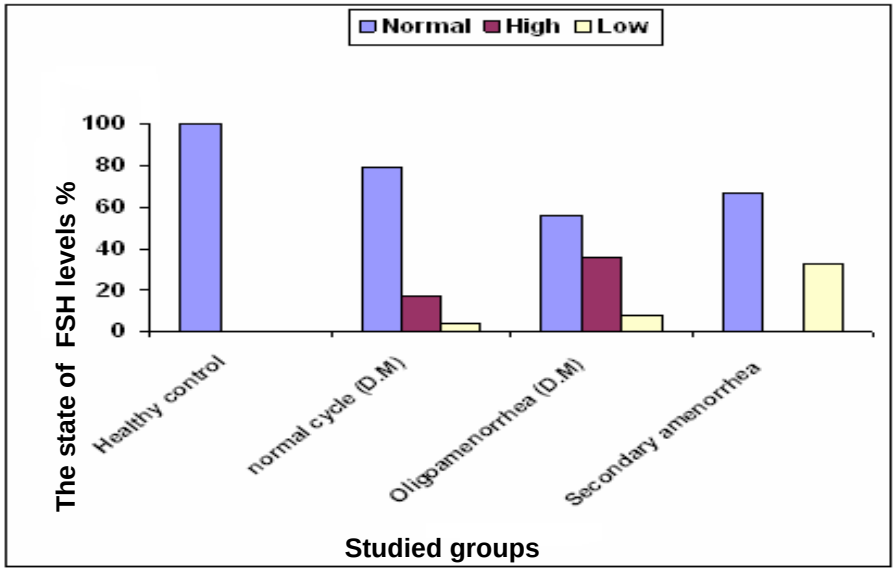
	%	100	0	0	100
Normal cycle DM1	N	23	1	0	24
	%	95.8	4.2	0	100
Oligoamenorrhea DM1	N	5	18	2	25
	%	20	72	8	100
Secondary amenorrhea DM1	N	8	1	3	12
	%	66.7	8.3	25	100
Total	N	36	20	5	61
	%	56	32.7	8.1	100
Comparison of significant			(P<0.01)		



ınder study.

Studied group		FSH level			Total
		Normal	High	Low	
Healthy control	N	35	0	0	35
	%	100	0	0	100
Normal cycle DM1	N	19	4	1	24

	%	79.2	16.7	4.2	100
Oligoamenorrhea DM1	N	14	9	2	25
	%	56	36	8	100
Secondary amenorrhea DM1	N	8	0	4	12
	%	66.7	0	33.3	100
Total	N	41	13	7	61
	%	67.2	21.3	11.4	100
Comparison of significant			(P<0.01)		



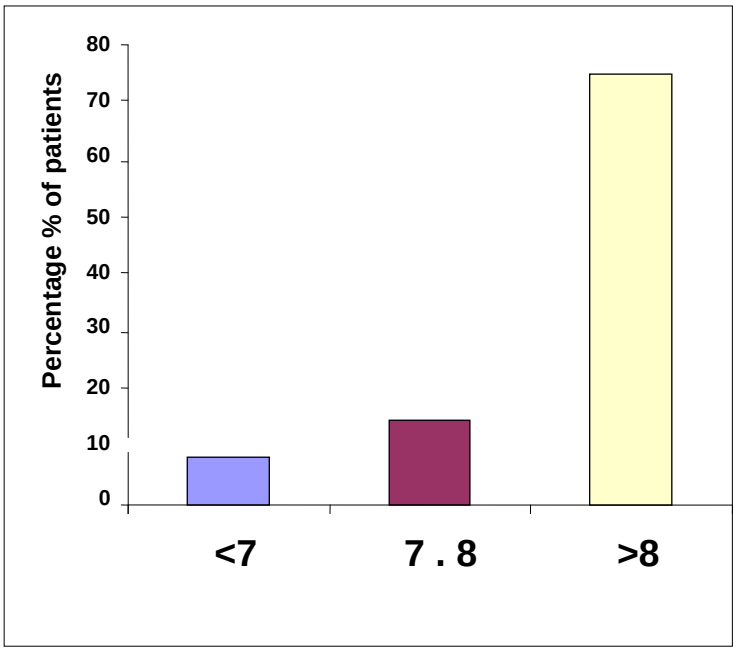
7. Glycated hemoglobin (HbA_{1c}) range

From table and figure (7) below we notice that there have been a highly significant differences (P<0.01) in HbA_{1c} ranges. (75.4%) of patients have >8% glycated hemoglobin which means that the majority of patients have a poor glycemic control according to American diabetes association (2005), while (14.8%) of the patients are considered to be fair glycemic control

having 7-8% glycated hemoglobin and (9.8%) of them are considered to be goals for HbA_{1c} in patients with diabetes was < 7.0%. People with diabetes and poor glycemic control have a significant incidence of complications from diabetes, including retinopathy and diabetic nephropathy [40].

Table & figure (7) Distribution of patients according to HbA_{1c}% range.

HbA1c range %[42]	N	%	Comparison of Significance by Kruskal-Wallis Test
<7	6	9.8	(P<0.01)
7-8	9	14.8	
>8	46	75.4	
Total	61	100	



8. HbA_1c range in various (LH & FSH) levels

In general, table and figure (8a) show a significant difference (P<0.05) between the three hormonal levels with HbA_{1C} ranges, in details; percentage normal LH level with HbA_{1C} range >8 was (86.1%), while the percentages of high and low LH levels with HbA_{1C}>8 were (60 %). From this we can notice an elevated HbA_{1C} range didn't affect hormonal levels but it may be

associated with it as in high and low levels. Distiller et. al, suggested that gonadotropic function depends on glucose metabolism and that may be related to a general impairment in protein synthesis which may occur in the insulinopenic state [26].

The result in table and figure (8b) below illustrated no significant difference between FSH levels (normal, high, and low) and HbA_{1C} ranges.

Table & figure (8a) Comparison study between LH level & HbA_1c range for diabetic patients.

LH level		HbA1c range			Total
		<7	7-8	>8	
Normal	N	2	3	31	36
	%	5.6	8.3	86.1	100
High	N	2	6	12	20
	%	10	30	60	100
Low	N	2	0	3	5
	%	40	0	60	100
Total	N	6	9	46	61
	%	9.8	14.8	75.4	100
Comparison of significant			(P<0.05)		

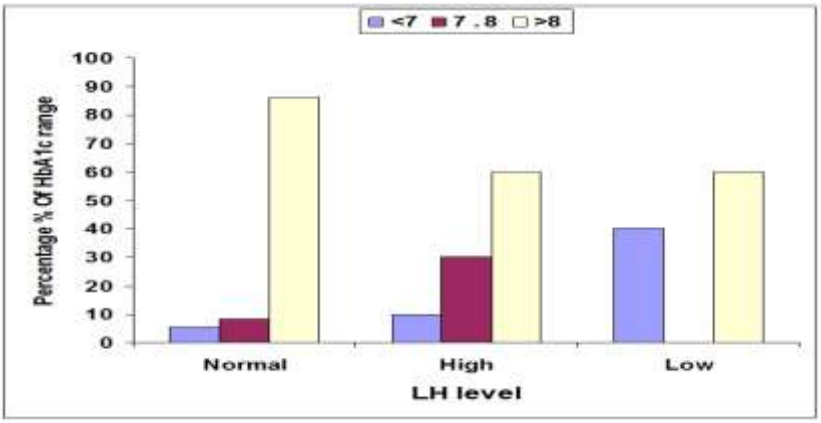
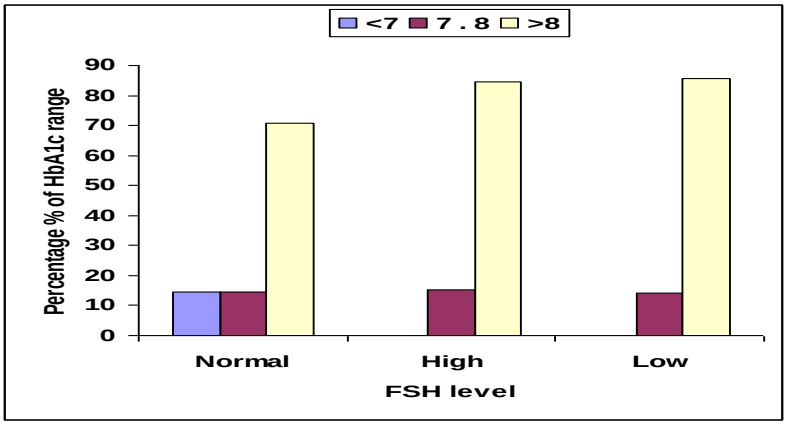


Table & A_{1c} range in the studied

FSH level		HbA1c range			Total
		<7	7-8	>8	
Normal	N	6	6	29	41
	%	14.6	14.6	70.7	100
High	N	0	2	11	13
	%	0	15.4	84.6	100
Low	N	0	1	6	7

	%	0	14.3	85.7	100
Total	N	6	9	46	61
	%	9.8	14.8	75.4	100
Comparison of significant			(P>0.05)		



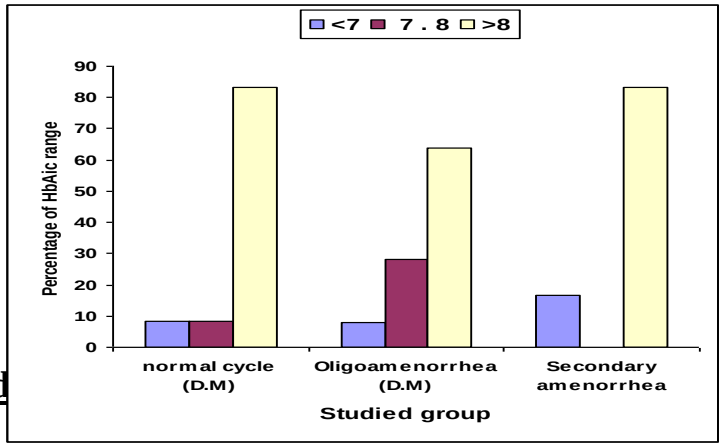
9. HbA_{1c} levels in the studied groups dividing them according to the menstrual frequency

The data analysis showed that there was a highly significant difference (P<0.01) between DM1 patients groups (normal cycle, oligoamenorrhea, and secondary amenorrhea) and HbA_{1C} rages in general as shown in table and figure (9); we can notice that the percentage of HbA_{1C} >8 was (83.3%) in the normal cycle DM1 patients and that means the poor glycemic control did not influence the menstruation in this group, the oligoamenorrhea group HbA_{1C} >8 percentage was (64%), and the secondary amenorrhea group (the self percentage with the normal cycle group was 83.3%).

Schroeder et. al., suggested that the glycemic control appears to influence menstruation in insulin-dependent diabetic adolescents and specialty those with elevated HbA_{1C} and diabetic ketoacidosis and significantly higher among diabetic adolescents with menstrual irregularity as compared to those with regular menses [32]. The different results in normal cycle group DM1 patients from the study of Schroeder et. al., may be attributed to the fact that our study was performed on adolescents and adults, while his study was limited to adolescents.

Table & figure (9) State of HbA_{1c} level in the groups under study.

Studied group		HbA1c range%			Total
		<7	7-8	>8	
normal cycle (DM1)	N	2	2	20	24
	%	8.3	8.3	83.3	100
Oligoamenorrhea (DM1)	N	2	7	16	25
	%	8	28	64	100
Secondary amenorrhea (DM1)	N	2	0	10	12
	%	16.7	0	83.3	100
Total	N	6	9	46	61
	%	9.8	14.8	75.4	100
Comparison of significant			(P<0.01)		



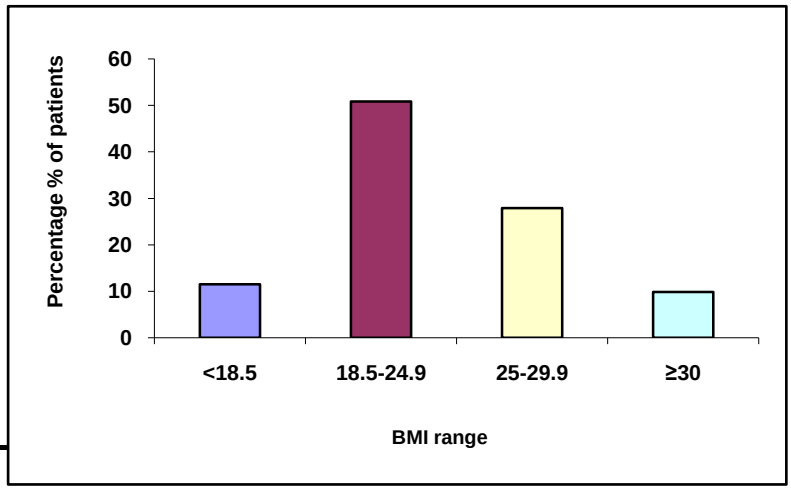
10. The bod

Although BMI does not show the difference between excessive fat and muscle, BMI is a measurement that is associated with the body fat .It also predicts the development of health problems related to excess weight. For these reasons, BMI is widely used by health care providers [41] [42]. From table and figure (10) we notice that there was a highly significant difference (P<0.01) between patients in BMI ranges, most of patients were in a healthy weight range (50.8%), the result agrees with [Danielson et. al.] [22], while the percentage of the patients with overweight was (27.9 %) and the obese patients was (9.8%). Rhodes et. al., suggested that Peripheral insulin action may promote weight gain by facilitating storage of metabolic fuels, thereby leading to hunger and increased caloric intake [43], and UKPDS group suggested that weight gain is a known complication of exogenous insulin treatment for type 1 diabetes [44].

(11.5%) of the patients was considered to be underweight; from the fact that insulin causes sugar to be stored in fat cells, lack of insulin output in type 1 diabetes affects glucose amount that reaches to the muscles and adipose tissues. Because glucose used becomes very inefficient, glucagon releases stored sugar from fat cells and from the liver. So symptoms such as weight loss will appear in DM1 [45].

Table & figure (10) Distribution of patients according to Body mass index BMI (Kg/m^2).

BMI (Kg/m^2)[44] [97]	N	%	Comparison of significant by Kruskal-Wallis Test
<18.5	7	11.5	(P<0.01)
18.5-24.9	31	50.8	
25-29.9	17	27.9	
≥30	6	9.8	
Total	61	100	



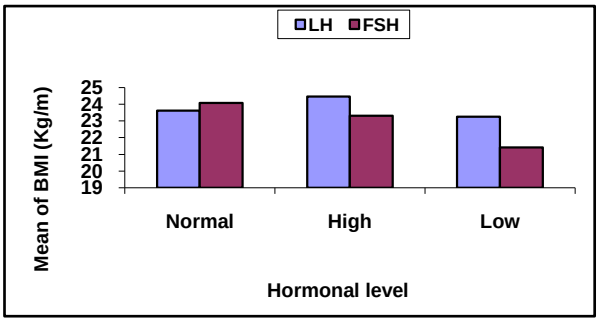
11. Body mass

Data illustrated in table and figure (11) show that there was no significant difference (P>0.05) between LH and FSH levels consecutively with mean BMI to each hormonal level, nearly BMI values with normal range canceled all the differentiations and made the result agree with [Strotmeyer et. al.; Ghazi.S.; and Danielson et. al.] [22] [25] [38].

Table & figure (11) Mean distribution of Body mass index (Kg/m^2) in relation to hormonal level (LH & FSH).

Hormonal level	LH		FSH	
	BMI Mean±SD	(Sig.)	BMI Mean±SD	(Sig.)
Normal	23.621±3.934	-	24.077±3.78	-
High	24.47±4.017	(P>0.05)	23.307±4.213	(P>0.05)
Low	23.26±7.954	(P>0.05)	21.414±7.326	(P>0.05)

High * Low	(P>0.05)	(P>0.05)



12. Body mass index mean in the studied groups dividing them according to the menstrual frequency

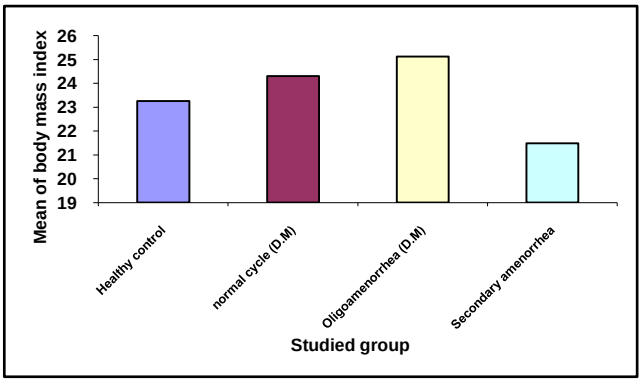
Result in table and figure (12) show that there was no significant difference (P>0.05) in mean BMI between the healthy control and type 1 diabetic patients with (normal cycle, oligoamenorrhea, and secondary amenorrhea) as in the study done by La Marco et al, who made a comparison between amenorrrhoeic and euamenorrhoeic women with insulin dependent diabetes [37].

(LSD) F- test in the same groups revealed a significant difference (P<0.01) between oligoamenorrhea group and secondary amenorrhea group, usually the secondary amenorrhea linked with the lowest BMI value and decreased body fat [46].

Table & figure (12) Mean distribution of Body mass index (Kg/m^2) in the studied groups.

Studied groups	N	BMI(Kg/m^2)	
		Mean±SD	(Sig.)
A-Healthy control	35	23.25± 3.42	-
B-normal cycle (DM1)	24	24.3±4.16	(P>0.05)
C-Oligomenorrhea(DM1)	25	25.11± 4.56	(P>0.05)
D-Secondary amenorrhea(DM1)	12	21.48± 4.59	(P>0.05)
Total	96		

Studied groups	LSD (F-test) Sig.
B * C	(P>0.05)
B * D	(P>0.05)
C * D	(P<0.05)



13. Body mass index mean in various HbA_{1c} range

The data demonstrated by table and figure (13) shows that there were no significant differences (P > 0.05) between mean BMI (Kg/m^2) and HbA_{1c} levels. LSD (F-test) shows that there was significant differences (P<0.05) between BMI of those with poor control and those with fair control, which clearly can be conformed on the poor glycemic control when leads to breakdown of protein in the skeletal muscles and loss of calories.

Table & figure (13) Mean distribution of Body mass index (Kg/m^2) in relation to HbA_{1c}% levels.

HbA1c% levels	N	Mean	Std. Deviation	Std. Error	Comparison of Significant by ANOVA
`<7	6	25.516	5.543	2.263	(P>0.05)
7-8	9	26.155	2.737	0.912	

>8	46	23.489	4.619	0.681	
Total	61				

HbA1c% levels		LSD (F-test)
<7	7-8	(P>0.05)
	>8	(P>0.05)
7-8	>8	(P<0.05)

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