Genetic and endrocrionological health risks of polycystic ovarian syndrome

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Abstract

Polycystic Ovarian Syndrome (PCOS) is a common endocrine disorder predominantly affecting women hormone levels during their childbearing years Clinical symptoms are diverse can be accompanied by hyperandrogenism, irregular/anovulation, infertility, weight gain, oily skin and increased metabolic risk diseases Data from PCOS patients were collected in order to evaluate the prevalence of this hormonal disorder and to assess several risk factors associated with it Moreover, our results revealed a significant altered relation with cortisol, LH and insulin hormones levels.

Keywords: PCOS, Prevalence, Hormone levels, Polycystic ovaries menstrual cycle, Infertility.

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Introduction

Polycystic Ovarian Syndrome (PCOS) is a common reproductive and endocrinologic disorder affecting more than 60%-70% of adult females of ages between 15 and 44 This heterogeneous disorder becomes more frequent in early reproductive stages, leading to multiple complications such as increased infertility risks, metabolic complications, depression, anxiety and endometrial cancer A patient diagnosed with PCOS has shown with at least 20 follicles per ovary with a size of 2-9 mm in diameter size [1-4]

PCOS can be described as enlarged bilateral ovaries with the development of avascular smooth, thickened capsule holding multiple cysts Various stages subcapsular follicles of atresia are present in the peripheral part of the ovary Characterized by dysfunctional ovulation, this heterogeneous disorder holds a biochemical hyperandrogenisim with a polycystic ovarian morphology leading to severe outcomes such as increased infertile risks, reduced pregnancy rates, epithelial cancer progression [5,6] The most evident feature of PCOS is hyperplasia of the theca stromal cells surrounding seized follicles This phenomenon is characterized by three main phenotypes and includes hyperandrogenism, polycystic ovaries, and ovulatory dysfunction [6-10] Metabolic complexities are another related issues associated with PCOS and include peripheral insulin resistance (present is 60%-80% of PCOS women), hyperinsulinemia, type 2 diabetes mellitus, increased body weight, physical inactivity, hirsutism, acne and anovulation The clinical outcomes of unresolved anovulation in PCOS women are severe and may result in infertility, abnormal vaginal and uterus bleeding, increased endometrial, breast cancer risks and cardiovascular diseases including elevated levels of increased triglyceride, reduced HDL and hypertension [11-14]

Our etiological understanding of the PCOS is currently incomplete Much evidence favors its relation with several predisposing and protective genetic variants suggesting more complex multigenic-associated inherited-key genes related to multiple a wide ranges of environmental factors At the ovarian level, insulin directly interacts with insulin growth factor type I receptors, stimulating the increase in abnormal ovarian steroidogenesis a consequence of inappropriate hypothalamic-pituitary-ovarian interaction [15-17]

Disordered gonadotropin is also another feature of PCOS, which is characterized by the increased levels of LH secretion and decreased levels of FSH production, leading to an increased LH-FSH ratio received by the pituitary gland This persistent condition increases anovulation risks due to the neuroendocrine expression deficiency of elevated LH frequency levels and relatively reduced FSH [18,19]

Another metabolic hallmark present in PCOS women is the alteration of both cortisol levels and adrenal androgen production Upon the inhibition of the hepatic SHBG production, the ovarian androgen levels increase both directly and indirectly upon insulin resistance This increase is also associated with obesity with low rate pregnancy and elevated sympathetic nerve activity [20]

Based on the severity of the symptoms affecting ovaries and ovulation, PCOS syndrome can be divided into main three grades These grades are dependent on several main features that are related to cysts in ovaries, levels of male hormones and irregular or skipped periods in adolescent women Grade I (Arwen stein Leventhal) symptoms are mainly characterized by severe obesity, first occurrence of menstrual cycle after puberty, Cushing syndrome, high prolactin and abnormal facial hair production (hirsutism) Grade II symptoms are less severe and appear as mild hirsutism, mild obesity, amenorrhea and cushing syndrome Grade III level is less severe and can be summarized by normal female hormone levels, no loss of irregular menstrual cycle and no weight gain However, the symptoms are directed towards the development of multi-follicles in the ovaries [21,22]

The purpose of this study is to estimate the prevalence of PCOS in adolescent Lebanese women its correlation with hormonal levels and its prevalence on the basis of genetic and endocrinological factors

Data Collection

The data was collected over a period of two months from a well-reputable hospital in Beirut The study aimed to reveal the frequency of adolescent women having PCOS with the possible factors that play a role in influencing and affecting its occurrence The women understudy were around 16 to forty-nine years of age without disclosing any information of the patients due to medical and personal confidentiality

The variables chosen to be assessed and measured on the PCOS patients were based in several entities including the relation between the occurrence of the disease and some genetic and endocrinological factors These variables were of the following: age, DHEAS, grades of the disease, prolactin, TSH, insulin, testosterone, FSH, LH and cortisol hormones The data was entered into IBM SPSS Software to be organized and summarized in order to clearly analyze it and obtain a solid conclusion (Figures 1-10; Tables 1-10) [23]

Descriptive statistics

Table 1. *Age of female participants 0 patients did not provide their age, and the ages of the female clients under study range between 16 and 49.*

Age	N	Minimum	Maximum	Mean	Std Deviation
	67	0	49	1807	15201
	Frequency	Percent			
0	27	386			
16	3	43			
18	4	57			
21	2	29			
22	2	29			
23	4	57			
24	3	43			
25	3	43			
26	2	29			
27	2	29			
28	2	29			
30	1	14			
31	1	14			
33	1	14			
34	1	14			
36	2	29			
37	1	14			
38	3	43			
40	3	43			
42	2	29			
49	1	14			
Total	70	100			

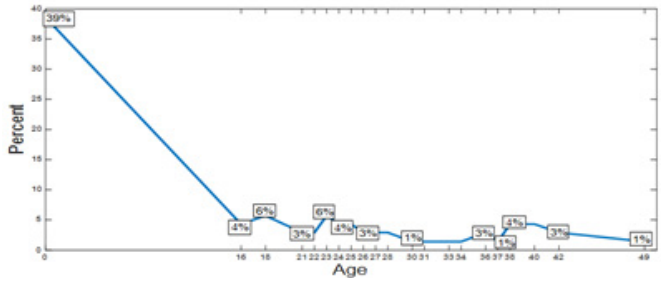

Figure 1. *Age of female participants 0 patients did not provide their age, and the ages of the female clients under study range between 16 and 49.*

TSH

Table 2. *Variable TSH levels The highest percentage in the samples under study showed 60% of TSH levels for normal, 33% for those with low TSH and 6% with the highest TSH levels.*

TSH	Frequency	Valid Percent %
Low	21	333
Normal	38	603
High	4	63
Total	63	100
Missing	7	
Total	70	

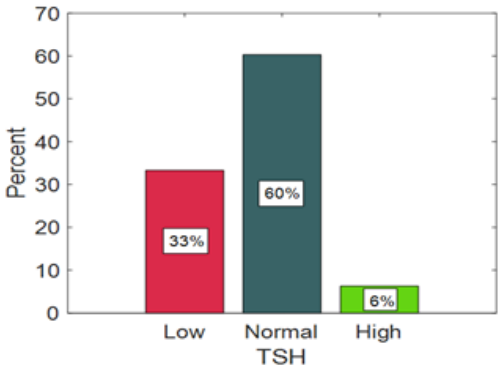

Figure 2. *Variable TSH levels The highest percentage in the samples under study showed 60% of TSH levels for normal, 33% for those with low TSH and 6% with the highest TSH levels.*

Prolactin

Table 3. *Variable prolactin levels 53% of females had normal prolactin levels, 31% with high result and 15% with low prolactin result.*

Prolactin	Frequency	Valid percent %
Low	10	149
Normal	36	537
High	21	313
Total	67	100
Missing	3	
Total	70	

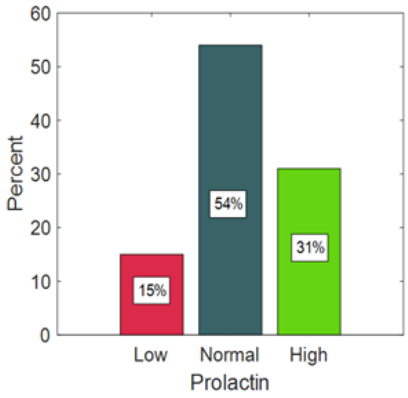

Figure 3. *Variable prolactin levels 53% of females had normal prolactin levels, 31% with high result and 15% with low prolactin result.*

Testosterone

Table 4. *Measuring testosterone levels 54% expressed low testosterone levels, 29% expressed normal and 18% expressed high levels.*

Testosterone	Frequency	Valid percent %
Low	30	536
Normal	16	286
High	10	179
Total	56	100
Missing	14	
Total	70	

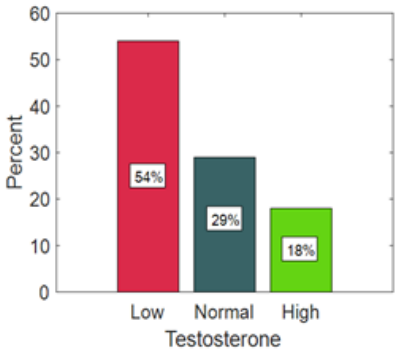

Figure 4. *Measuring testosterone levels 54% expressed low testosterone levels, 29% expressed normal and 18% expressed high levels.*

Cortisol

Table 5. *Variable cortisol levels 60% had normal cortisol level, 38% with high, 2% with low.*

Cortisol	Frequency	Valid percent %
Low	1	22
Normal	27	60
High	17	378
Total	45	100
Missing	25	
Total	70	

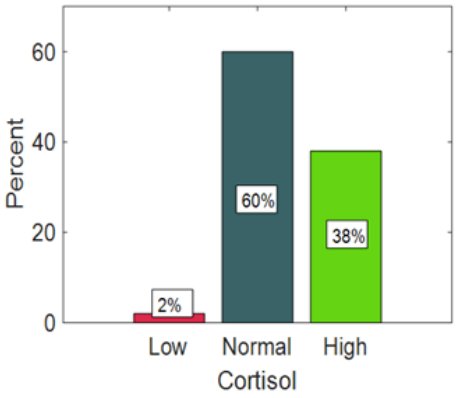

Figure 5. *Variable cortisol levels 60% had normal cortisol level, 38% with high, 2% with low.*

FSH

Table 6. *Various FSH results of selected samples 76% had normal result, 17% high, 7% low.*

FSH	Frequency	Valid percent %
Low	2	69
Normal	22	759
High	5	172
Total	29	100
Missing	41	
Total	70	

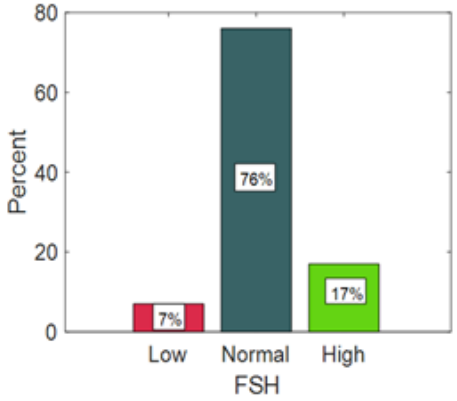

Figure 6. *Various FSH results of selected samples 76% had normal result, 17% high, 7% low.*

LH

Table 7. *Measuring LH levels 40% had normal test, 44% with low and 16% with high levels.*

LH	Frequency	Valid percent %
Low	11	44
Normal	10	40
High	4	16
Total	25	100
System	45	
Total	70	

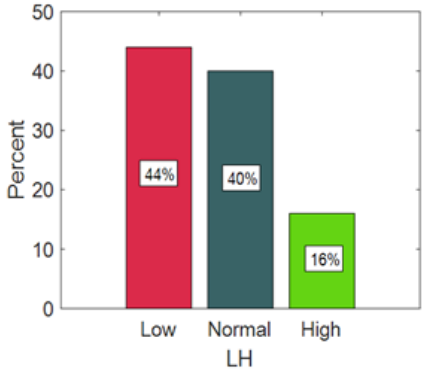

Figure 7. *Measuring LH levels 40% had normal test, 44% with low and 16% with high levels.*

Insulin

Table 8. *Test results for insulin in our sample 55% had normal, 15% with high and 29% expressing low levels.*

Insulin	Frequency	Valid percent %
Low	19	292
Normal	36	554
High	10	154
Total	65	100
Missing	5	
Total	70	

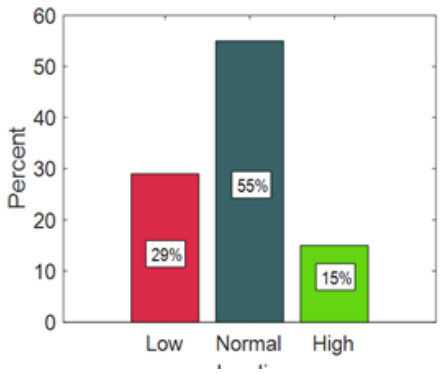

Figure 8. *Test results for insulin in our sample 55% had normal, 15% with high and 29% expressing low levels.*

DHEAS

Table 9. *Test results for DHEAS in our sample. 67.2% showed normal levels, 6.3% with high levels and 26.6% low levels.*

DHEAS	Frequency	Valid percent %
Low	17	266
Normal	43	672
High	4	63
Total	64	100
Missing	6	
Total	70	

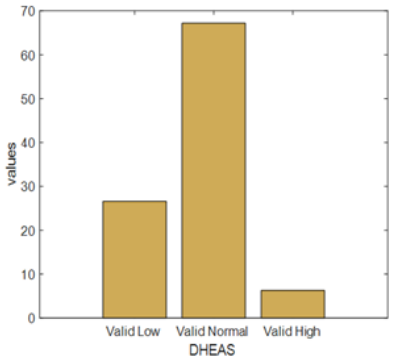

Figure 9. *Test results for DHEAS in our sample. 67.2% showed normal levels, 6.3% with high levels and 26.6% low levels.*

Grade of the disease (I, II, III)

Table 10. *Test results for grade of the disease (I, II, III). The majority of tested samples belong to Grade III 65%, 35% of the patients represents Grade II and with the absence of Grade I.*

Grade	Frequency	Valid percent %
Grade II	24	34.8
Grade III	45	65.2
Total	69	100
Missing	1	
Total	70	
Total	70	

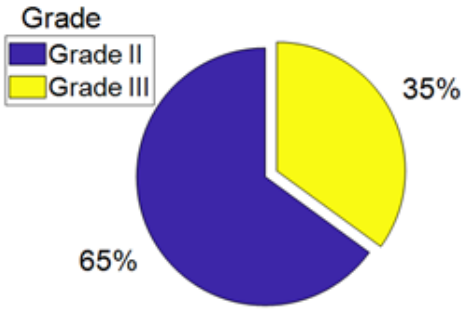

Figure 10. *Test results for grade of the disease (I, II, III). The majority of tested samples belong to Grade III 65%, 35% of the patients represents Grade II and with the absence of Grade I.*

Inferential Statistics

Hypothesis

Chi-square test was used to quantify different variables, using a dependent variable grade, and independent variables tests According to the chi-square test, p-value=000 thus p-value<005 which implies that it was significant, therefore rejecting H0 and accepting H1 (Tables 11-20)

H0: Showed no relation between grade and tests

H1: Showed is a relation between grade and tests

*Grade*TSH*

Table 11. *Inferential statistics of Grade*TSH. 2 cells (33.3%) had expected count less than 5. The minimum expected count is 1.40. a: Age.*

Grade		TSH			Total	p-value	Decision
Grade II	Count	Low	Normal	High			
		11	9	2	22		
	Percent	50.00%	40.90%	9.10%	100.00%		
Grade III	Count	10	29	2	41	0.070>0.05	There was no relation between Grade and TSH, they weren't significant, H0 was accepted
	Percent	24.40%	70.70%	4.90%	100.00%		
Total	Count	21	38	4	63		
	Percent	33.30%	60.30%	6.30%	100.00%		
Chi-square tests							
		Value	df	Asymptotic significance (2-sided)			
Pearson chi-square		5.328a	2	0.07			
Likelihood ratio		5.303	2	0.071			
Linear-by-linear association		1.991	1	0.158			
N of valid cases		63					

*Grade*Prolactin*

Table 12. *Inferential statistics of Grade*Prolactin. 1 cells (16.7%) had expected count less than 5. The minimum expected count is 3.48. a: Age.*

Grade		**Prolactin**			**Total**	**p-value**	**Decision**
Grade II	Count	Low	Normal	High	23	0.233>0.05	There was no relation between grade and prolactin, they weren't significant,
		4	9	10			
	Percent	17.40%	39.10%	43.50%	100.00%		
Grade III	Count	6	26	11	43		
	Percent	14.00%	60.50%	25.60%	100.00%		
Total	Count	10	35	21	66		
	Percent	15.20%	53.00%	31.80%	66		
Chi-square tests							
		Grade II	df	Asymptotic significance (2-sided)			
Pearson chi-square		2.912a	2	0.233			
Likelihood ratio		2.91	2	0.233			
Linear-by-linear association		0.698	1	0.403			
N of valid cases		66					

*Grade*Testosterone*

Table 13. *Inferential statistics of Grade*Testosterone. 2 cells (33.3%) had expected count less than 5. The minimum expected count is 3.04. a: Age.*

Grade		**Testosterone**			**Total**	**p-value**	**Decision**
Grade II	Count	Low	Normal	High	17	0.155>0.05	There was no relation between grade and testosterone, they weren't significant, H0 was accepted
		12	2	3			
	Percent	70.60%	11.80%	17.60%	100.00%		
Grade III	Count	18	14	7	39		
	Percent	46.20%	35.90%	17.90%	100.00%		
Total	Count	30	16	10	56		
	Percent	53.60%	28.60%	17.90%	100.00%		
Chi-square tests							
		Value	df	Asymptotic significance (2-sided)			
Pearson chi-square		3.733a	2	0.155			
Likelihood ratio		4.098	2	0.129			
Linear-by-linear association		1.213	1	0.271			
N of valid cases		56					

*Grade*Cortisol*

Table 14. *Inferential statistics of Grade*Cortisol. 2 cells (33.3%) had expected count less than 5. The minimum expected count is 0.40. a: Age.*

Grade		**Cortisol**			**Total**	**p-value**	**Decision**
Grade II	Count	Low	Normal	High	18	0.009<0.05	There was a relation between Grade and Cortisol they were significant, H1 was accepted
		1	6	11			
	Percent	5.60%	33.30%	61.10%	100.00%		
Grade III	Count	0	21	6	27		
	Percent	0.00%	77.80%	22.20%	100.00%		
Total	Count	1	27	17	45		
	Percent	2.20%	60.00%	37.80%	100.00%		
Chi-square tests							
		Value	df	Asymptotic significance (2-sided)			
Pearson chi-square		9.379a	2	0.009			
Likelihood ratio		9.892	2	0.007			
Linear-by-linear association		4.289	1	0.038			
N of valid cases		45					

*Grade*FSH*

Table 15. *Inferential statistics of Grade*FSH. 4 cells (66.7%) had expected count less than 5. The minimum expected count is 0.86. a: Age.*

Grade		FSH			Total	p-value	Decision
Grade II	Count	Low	Normal	High		0.971>0.05	There was no relation between FSH and Grade, they weren't significant, H0 was accepted
		1	9	2	18		
	Percent	8.30%	75.00%	16.70%	100.00%		
Grade III	Count	1	12	3	16		
	Percent	6.30%	75.00%	18.80%	100.00%		
Total	Count	2	21	5	28		
	Percent	7.10%	75.00%	17.90%	100.00%		
Chi-square tests							
		Value	df	Asymptotic significance (2-sided)			
Pearson Chi-square		.058a	2	0.971			
Likelihood ratio		0.058	2	0.971			
Linear-by-linear association		0.048	1	0.826			
N of valid cases		28					

*Grade*LH*

Table 16. *Inferential statistics of Grade*LH. 4 cells (66.7%) had expected count less than 5. The minimum expected count is 1.67. a: Age.*

Grade		LH			Total	p-value	Decision
Grade II	Count	Low	Normal	High		0.049<0.05	There was a relation between Grade and LH, they were significant so, H1 was accepted and H0 was rejected.
		6	1	3	10		
	Percent	60.00%	10.00%	30.00%	100.00%		
Grade III	Count	1	12	3	16		
	Percent	6.30%	75.00%	18.80%	100.00%		
Total	Count	11	9	4	24		
	Percent	45.80%	37.50%	16.70%	100.00%		
Chi-square tests							
		Value	df	Asymptotic significance (2-sided)			
Pearson chi-square		6.036a	2	0.049			
Likelihood ratio		6.665	2	0.036			
Linear-by-linear association		0.002	1	0.963			
N of valid cases		24					

*Grade*Insulin*

Table 17. *Inferential statistics of Grade*Insulin. 1 cells (16.7%) had expected count less than 5. The minimum expected count is 3.54. a: Age.*

Grade		Insulin			Total	p-value	Decision
Grade II	Count	Low	Normal	High		0.000<0.05	There was a relation between Grade and Insulin, they were significant, H0 was accepted
		11	4	8	10		
	Percent	47.80%	17.40%	34.80%	100.00%		
Grade III	Count	8	32	2	42		
	Percent	19.00%	76.20%	4.80%	100.00%		
Total	Count	19	36	10	65		
	Percent	29.20%	55.40%	15.40%	100.00%		
Chi-square tests							
		Value	df	Asymptotic significance (2-sided)			
Pearson chi-square		22.194a	2	0			
Likelihood ratio		23.485	2	0			
Linear-by-linear association		0.005	1	0.942			
N of valid cases		65					

*Grade*DHEAS*

Table 18. *Inferential statistics of Grade*DHEAS. 2 cells (33.3%) had expected count less than 5. The minimum expected count is 1.31. a: Age.*

Grade		DHEA-S			Total	p-value	Decision
Grade II	Count	Low	Normal	High		0.210>0.05	There was no relation between Grade and DHEA's, they weren't significant, H0 was accepted
		8	11	2	21		
	Percent	38.10%	52.40%	9.50%	100.00%		
Grade III	Count	9	32	2	43		
	Percent	20.90%	74.40%	4.70%	100.00%		
Total	Count	17	43	4	64		
	Percent	26.60%	67.20%	6.30%	100.00%		
Chi-square tests							

	Value	df	Asymptotic significance (2-sided)
Pearson chi-square	3.121a	2	0.21
Likelihood ratio	3.048	2	0.218
Linear-by-linear association	0.732	1	0.392
N of valid cases	64		

Case processing summary

Table 19. *Case processing summary. *Correlation: Abivariate analysis that measures the strength of association between two variables and the direction of the relationship. In terms of the strength of relationship, the value of the correlation coefficient varies between +1 and -1. A value of ± 1 indicates a perfect degree of association between the two variables. As the correlation coefficient value goes towards 0, the relationship between the two variables will be weaker.*

	Cases					
	Valid		**Missing**		**Total**	
	N	Percent	N	Percent	N	Percent
Grade*TSH	63	90.00%	7	10.00%	70	100.00%
Grade*Prolactin	66	94.30%	4	5.70%	70	100.00%
Grade*DHEA-S	64	91.40%	6	8.60%	70	100.00%
Grade*Testosterone	56	80.00%	14	20.00%	70	100.00%
Grade*Cortisol	45	64.30%	25	35.70%	70	100.00%
Grade*FSH	28	40.00%	42	60.00%	70	100.00%
Grade*LH	24	34.30%	46	65.70%	70	100.00%
Grade*Insulin	65	92.90%	5	7.10%	70	100.00%

Correlations between all hormonal levels

Table 20. *Correlations between all hormonal levels. *: Correlation is significant at the 0.05 level (2-tailed). **: Correlation is significant at the 0.01 level (2-tailed).*

PMNv			**Grade**	**TSH**	**Prolactin**	**DHEA-S**	**Testosterone**	**Cortisol**	**FSH**	**LH**
Spearman's rho	Grade	Correlation coefficient	1	0.203	-0.117	0.124	0.178	-.343*	0.041	0.073
		Sig. (2-tailed)	.	0.111	0.348	0.33	0.189	0.021	0.835	0.735
		N	69	63	66	64	56	45	28	24
	TSH	Correlation coefficient	0.203	1	.309*	-0.014	0.137	0.236	0.032	-0.105
		Sig. (2-tailed)	0.111	.	0.014	0.913	0.332	0.132	0.879	0.642
		N	63	63	63	59	52	42	25	22
	Prolactin	Correlation coefficient	-0.117	.309*	1	0.058	0.223	0.035	-0.025	-0.158
		Sig. (2-tailed)	0.348	0.014	.	0.657	0.106	0.825	0.9	0.462
		N	66	63	67	62	54	43	27	24
	DHEA-S	Correlation coefficient	0.124	-0.014	0.058	1	0.21	-0.168	-0.161	.551**
		Sig. (2-tailed)	0.33	0.913	0.657	.	0.131	0.293	0.443	0.008
		N	64	59	62	64	53	41	25	22
	Testosterone	Correlation coefficient	0.178	0.137	0.223	0.21	1	-0.303	-0.312	0.449
		Sig. (2-tailed)	0.189	0.332	0.106	0.131	.	0.057	0.193	0.071
		N	56	52	54	53	56	40	19	17
	Cortisol	Correlation coefficient	-.343*	0.236	0.035	-0.168	-0.303	1	0.239	-.722**
		Sig. (2-tailed)	0.021	0.132	0.825	0.293	0.057	.	0.339	0.004
		N	45	42	43	41	40	45	18	14
	FSH	Correlation coefficient	0.041	0.032	-0.025	-0.161	-0.312	0.239	1	-.522**
		Sig. (2-tailed)	0.835	0.879	0.9	0.443	0.193	0.339	.	0.007
		N	28	25	27	25	19	18	29	25
	LH	Correlation coefficient	0.073	-0.105	-0.158	.551**	0.449	-.722**	-.522**	1
		Sig. (2-tailed)	0.735	0.642	0.462	0.008	0.071	0.004	0.007	.
			24	22	24	22	17	14	25	25
	Insulin	Correlation coefficient	0.029	0.056	-.393**	-0.238	-0.011	-0.197	-0.013	.415*
		Sig. (2-tailed)	0.82	0.674	0.002	0.067	0.936	0.194	0.948	0.049
		N	65	59	62	60	52	45	27	23

The following significant results from our sample were studied: age, DHEAS, grades of the disease, prolactin, TSH, insulin, testosterone, FSH, LH and cortisol hormones In our findings, the PCOS disease was shown to be directly affecting hormone fluctuations Most of our PCOS patients belonged to Grade III with an average of 65% The remaining 35% was on Grade II category with the absence of Grade I Our inferential statistics showed a significant correlation between the grade of the disease from one end and the expression levels of cortisol, LH and insulin hormones The remaining variables (prolactin, TSH, FSH and DHEA's) showed no significant alteration with respect to grade categories

There was a significant down correlation (-343) between Grade and cortisol value, with a significant value 0021<005, indicating that the compared variables were directly correlated to each other However, a low correlation (0203) was indicated between Grade and TSH levels with significant values of 0021<005 and 0111>005 These results indicate that there was no correlation between Grade and TSH Moreover, a similar outcome occurred between Grade and prolactin levels showing low correlation (-0117) with a significant value 0348>005 indicating that these variables and not directly related There was a positive low correlation between Grade and DHEA-S (0124) with a significant value 0330>005, indicating that these two variables were low correlated and not related Similarly positive low correlations were also observed when Grade was individually compared with Testosterone, FSH and insulin Each comparison showed 0178 with a significant value 0189>005, a 0073 with a significant value 0753>005 significantly and a 0029 with a significant value 0820>005 respectively These findings indicate that these variables were low correlated and not related [24]

Conclusion

Polycystic ovarian Syndrome has a significant relation with the expression levels of cortisol, LH and insulin hormones This syndrome disrupts the menstrual cycle during the reproductive stages, making it hard for women hard to get pregnant PCOS is mainly caused my many factors such as obesity, hyperandrogenism, polycystic ovaries, and ovulatory dysfunction As a result, multiple reproductive and metabolic complications arise such as infertility, menstrual bleeding problems (ranging from amenorrhea to dysfunctional uterine bleeding), and increased risks of endometrial cancer, breast carcinoma and cardiovascular diseases In summary, this syndrome disrupts the menstrual cycle, making it hard for women hard to get pregnant Moreover, high levels LH hormones Therefore, women nowadays should be more aware of PCOS symptoms due to its mortal risks The benefits of prolonged treatments such as life style changes, use of birth control pills and other medications should be strongly considered and closely discussed with patients to restore back normal menstrual cycle

Consent for Publication

Not applicable

Competing Interests

The authors declare there are no competing interests

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