

Study of Occurrence of Polycystic Ovarian Syndrome Among Infertile Women

Hanaa Rahman Eleawi*, Enas Talib Abdul-Karim**,
Anam Rasheed AL- Salihi***

ABSTRACT:

BACKGROUND:

Most women with polycystic ovary syndrome PCOS don't even know that they have it ,and do not get a diagnosis until they begin trying to get pregnant.

OBJECTIVE:

To identify the prevalence of the polycystic ovary syndrome (PCOS) among infertile women attending the Institute of Embryo Research and Infertility Treatment in AL-Kadhymia\Baghdad, and to identify some of the common characteristics of infertile women with PCOS and others without PCOS .

METHODOLOGY:

A cross sectional study was conducted for about four months,during which a review of records of all the women attending the Institute during the year 2010 (six hundred women) .

RESULTS:

Results showed that the most common factors of infertility in infertile women is the PCOS, PCOS had a higher frequency among women aged 20-29 years, Slightly higher frequency of diabetes mellitus and hypertension among them than other group. higher frequency of acne & hirsutism among the PCOS cases than other causes group, and a higher frequency of increased prolactin level& LH level in the PCOS cases.

CONCLUSION:

PCOS infertility comprises more than one fourth of causes of infertility and is associated mainly with primary infertility & among younger age group(20-29years) .

KEYWORD: infertility, polycystic ovarian syndrome

INTRODUCTION:

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age^(1, 2), it is a condition associated with chronic anovulation, insulin resistance, and androgen excess⁽²⁾. Affected individuals typically present to clinical attention during evaluation for infrequent menses, infertility, and/or hirsutism^(3,4, 5). The prevalence of PCOS among women of reproductive age in the general population has been estimated at 4% to 12%⁽⁴⁾, the prevalence and characteristics of women with PCOS among broader, ethnically diverse populations and within usual care settings are less well understood, it appear to be higher (from 37% to 90%) in women with menstrual abnormalities

and also is increased in the presence of certain diseases⁽⁵⁾.

In addition to reproductive and hyperandrogenic concerns, PCOS is also associated with a number of metabolic perturbations that ultimately may contribute to an excess risk for cardiovascular events. Women with PCOS are more likely to be insulin resistant, overweight, and obese, and several studies have demonstrated that PCOS is associated with an increased risk of glucose intolerance and type 2 diabetes mellitus, independent of body mass index (BMI)⁽⁶⁾. Finally, a growing body of evidence suggests an association between PCOS and hypertension and markers of subclinical atherosclerosis and vascular dysfunction^(5, 7,8, 9).

Excess insulin appears to increase production of androgen. Levels of androgen that are higher than normal can lead to acne, excessive hair growth, weight gain, and problems with ovulation⁽⁵⁾. The cutaneous manifestations of increased androgenic

*Al-karkh Health Directorate of Baghdad.

**Department of Family and Community Medicine\College of Medicine\Al-Nahrain University.

***The Institute of Embryo Research and Infertility Treatment\ AL-Nahrain University.

POLYCYSTIC OVARIAN SYNDROME

hormones are hirsutism, acne, seborrhea, alopecia, obesity, and acanthosis nigricans⁽²⁾. On the basis of the National Institutes of Health (NIH) meeting in 2003, any two of the three are sufficient to confirm the diagnosis of PCOS⁽¹⁰⁾ specific morphology of polycystic ovaries in ultrasonography findings,⁽¹¹⁾ hyperandrogenism (biochemical or clinical), and oligo- or amenorrhoea.⁽¹²⁾

AIM OF THE STUDY:

To identify the prevalence of the polycystic ovary syndrome (PCOS) among infertile women attending the Institute of Embryo Research and Infertility Treatment in AL-Kadhymia/Baghdad and to identify some of the common characteristics of infertile women with PCOS and others without PCOS.

PATIENTS & METHODS:

Site of Study:-

The present study was carried out in The Institute of Embryo Research and Infertility Treatment in AL- Kadhimiya.

Agreement to conduct the study was obtained from the Iraqi Scientific Council of Family and Community Medicine and approved by the Ministry of Higher Education and Scientific Research\Al-Nahrain University\Institute of Embryo Research & Treatment.

This cross sectional study was conducted for about four months from beginning of January 2011 to the end of April 2011 including all women attending the Institute during the period of one year from beginning of January 2010 to the end of December 2010, where Six hundred women were studied by retrieving their files for one year from beginning of January 2010 to the end of December 2010.

Data retrieved from the files were the following.

1-Demographic data like age, age at marriage, occupation, educational status in years, address, health data on infertile woman including, duration of marriage, duration of infertility, gravida, Parity & abortion.

Body mass index (BMI) dropped from the study because in

Some of the records these information were not recorded

2-Type of infertility whether primary or secondary.

3- History of previous use of any contraception.

4-Medical history : acne, hirsutism, diabetes mellitus, hypertension, and galactorrhea

5- Menstrual history : Regularity of menstruation ; any menstrual disturbance like secondary amenorrhoea or heavy menstrual blood loss

Dysmenorrhoea: is defined as women suffering from discomfort or pain with periods⁽¹³⁾.

Oligomenorrhoea: is defined as menstrual cycles of more than 36 days or fewer than 9 menstrual periods per calendar year⁽¹⁴⁾.

6-Ultrasound (both abdominal and vaginal) findings: ovarian size, number of follicles in the plane line.

7-Hormonal assay :LH (normal range =1-10 mIU/ml),FSH(normal range =3-8mIU/ml)in the follicular phase, prolactin level in premenopausal(1.3-20 ng/ml)⁽¹³⁾.

8. Other blood investigation for certain diseases like diabetes mellitus, hypertension, thyroid disease

9- Causative factor of infertility :PCOS, other ovarian disorders, cervical factor, uterine-tubal factors, male factor, unexplained infertility.

Inclusion criteria:-

All files of women who had been registered in the Institute for the period of one year from beginning of January 2010 to the end of December 2010 were included.

women were enrolled in the study whether they had primary or secondary infertility.

Exclusion criteria:-

Exclusion criteria of related disorders: like Cushing syndrome, Virilizing tumor of adrenal or ovarian tumors.

Limitation of the study:-

Like other studies using records, missing information was a disabling point in the study. According to the data collected, infertile females were divided into those who were having PCOS (174 females) and those with other causes of infertility (426 females).

Statistical analysis :-

Data were coded & entered to computer for statistical analysis and was conducted by using SPSS program (Statistical Package for Social Science) version 18. All data were arranged in frequencies & associations between variables were tested by using the Chi-square & p value ≤ 0.05 was considered as significant.

Results

Results showed that the most common factors of infertility were male factors followed by PCOS, while Unexplained factors formed only 3% (table 1).

PCOS cause of infertility had a significantly higher frequency among women aged 20-29 years ($P=0.0001$). Slightly higher frequency of housewives was found in the PCOS cases & slightly higher frequency of workers in the other causes group with no statistically significant

POLYCYSTIC OVARIAN SYNDROME

association ($P=0.086$), there was higher frequency of PCOS infertility (60.9%) in low educational level (1-6 years) group, the infertility was more in urban than rural area with no statistically significant association (table 2). There was higher frequency of primary infertility among the PCOS infertility group and the duration of infertility of <5 years was more in PCOS infertility group than among other causes of infertility group with a significant difference between the two groups ($P=0.004$, $P=0.018$ respectively) (table 3).

Table 4 showed slightly higher frequency of diabetes mellitus and hypertension among the infertile women with PCOS than other group with no statistical significance between the two groups.

Table 5 showed higher frequency of acne & hirsutism among the PCOS cases than other causes group so the Chi-square test showed statistically significant association regarding acne

& hirsutism ($P=0.0001$ and $P=0.0001$ respectively), while galactorrhea had slightly higher percentage among the other causes group of infertility than PCOS group, the Chi-square test showed no statistically significant association ($P=0.063$) & showed that all symptoms were found more frequently among PCOS group than other causes group. The Chi-square test showed statistically significant association regarding Irregular menstrual cycle $P=0.0001$, Oligomenorrhea $P=0.0001$ & Dysmenorrhea $P=0.0001$.

Table 6 showed a higher frequency of increased prolactin level & LH level in the PCOS cases than other causes group, while there was increase level of FSH in other causes group than the PCOS group the Chi-square test showed statistically significant association in LH & Prolactin level (LH $P=0.0001$, Prolactin $P=0.0001$). the Chi-square test showed no statistically significant association in FSH level (FSH $P=0.005$).

Table 1: Distribution of cases of infertility by causes of infertility.

Causes of infertility	Frequency	%
PCOS cause of infertility	174	29.0
Other ovulatory factors	80	13.3
Cervical factors	26	4.3
Uterine tubal factors	58	9.7
*Male factors	246	41.0
Unexplained factors	18	3.0

*2 couples had PCOS cause of infertility & male factor

Table 2: Distribution of cases of infertility by different variables.

Variables	PCOS cause		Other causes		P-value
	N=174	%	N=426	%	
Age					$P=0.0001$
<20	10	5.7	18	4.2	
20-29	96	55.2	150	35.4	
30-39	58	33.3	206	48.2	
≥ 40	10	5.8	52	12.2	
Occupation					$P=0.086$
Housewife	150	86.1	342	80.3	
Worker	24	13.9	84	19.7	
Educational level					$P=0.011$
1-6 years	106	60.9	226	53	
7-12 years	62	35.6	154	36.1	
>12 years	6	3.4	46	10.7	
Residency					$P=0.659$
Urban	168	96.5	408	95.7	
Rural	6	3.4	18	4.2	

The Chi-square test used in this table

Table 3: Distribution of cases of infertility by type and duration of infertility.

Variables	PCOS cause		Other causes		P-value
	N=174	%	N=426	%	
Type of infertility					P=0.004
Primary	128	73.6	260	61.0	
Secondary	46	26.	166	39.0	
Duration of infertility(years)					P=0.018
<5	138	79.3	290	68.2	
5-9	30	17.2	106	24.8	
≥ 10	6	3.4	30	7.0	

The Chi-square test used in this table

Table 4: Distribution of cases of infertility by medical conditions.

Variables	PCOS cause		Other causes		P-value
	N=174	%	N=426	%	
Diabetes mellitus					P=0.439
Yes	4	2.3	6	1.4	
No	170	97.7	420	98.6	
Hypertension					P=0.248
Yes	6	3.4	8	1.9	
No	168	96.6	418	98.1	

The Chi-square test used in this table

Table 5: Distribution of cases of infertility by signs and Symptoms

Signs	PCOS cause		Other causes		P-value
	N=174	%	N=426	%	
Acne	116	66.7	16	3.8	P=0.0001
Hirsutism	144	82.8	24	5.6	P=0.0001
Galactorrhea	40	22.9	130	30.6	P=0.063
Symptoms	N=174	%	N=426	%	
Irregular menstrual cycle	104	59.8	106	24.9	P=0.0001
Oligomenorrhea	108	62.0	68	15.9	P=0.0001
Dysmenorrhea	150	86.2	300	70.2	P=0.0001

The Chi-square test used in this table.

Table 6: Distribution of cases of infertility by hormonal assay.

Hormonal assay	PCOS cause		Other causes		P-value
	N=174	%	N=426	%	
LH level					P=0.0001
Decreased	0	0	28	6.6	
Normal	16	9.2	274	64.3	
Increased	158	90.8	124	29.1	
FSH level					P=0.005
Decreased	14	8.0	44	10.3	
Normal	150	86.2	320	75.1	
Increased	10	5.74	62	14.5	
Prolactin level					P=0.0001
Decreased	0	0	4	0.9	
Normal	82	47.1	280	65.7	
Increased	92	52.9	142	33.3	

The Chi-square test used in this table

DISCUSSION:

This study is the first study that described the prevalence of PCOS among infertile women attending the Institute of Embryo Research and Infertility Treatment in AL- Kadhimiya \Baghdad city. PCOS was found to be the most prevalent type of infertility after male causes. PCOS infertility was 29%, this agreed with study done in Spain where the prevalence of PCOS was 28.3% in overweight or obese women⁽¹⁵⁾, in study that done in Kamal Al-Samarae hospital in Baghdad it was 24.1%⁽¹⁶⁾ this result does not agree with the study done in India which found that the PCOS is the most prevalent type of infertility 46.50%⁽¹⁷⁾, and in study done in Tikrit Teaching Hospital PCOS infertility was found to be 73.3%⁽¹⁸⁾ & but in other studies in a sample of an Iranian population, in unselected Caucasian women from Spain & sample of the Greek Island of Lesbos population the prevalence of PCOS were 14.6%, 6.5%, 6.77% respectively^(19, 20, 21). The result showed that nearly 41% of infertility were due to male causes and this does not agree with the study done in Kamal Al-Samarae hospital \Baghdad, which found about 4.4% were due to male infertility⁽¹⁶⁾. which may be due to many reasons like low socioeconomic, infection, poverty or the occupation of men & the psychological cause all these factors may lead to increase of male infertility.

According to the age groups there was higher frequency of PCOS infertility among younger age group (20-29 years) & this agrees with studies in India & Grampian & Kamal Al-Samarae hospital^(17,22, 16) & this may be due to PCOS is a syndrome of adolescence^(23,24).

In the present study the higher percentage of PCOS cause of infertility found among housewives (86.20%) than workers women, this agree with study done in Basrah which found that about 85% of infertile women were housewives⁽²⁵⁾ & with study that done in south India in three districts which found in Kanyakumari, Thirunelveli and Thiruvananthapuram the infertility was more in unemployed women (76.64%, 78.77% and 70.18% respectively)⁽²⁶⁾ this probably due to the fact that women not working have higher body weight than working women, and the stress of infertility per se increase the body weight⁽²⁶⁾.

The educational level of women has a role in infertility and there is high percentage of PCOS infertility (60.9%) in low educational level (1-6 years) than in other educational levels, this agree with study done in Basrah which found high

percentage of low educational level in infertile women⁽²⁰⁾.

In this study women with PCOS infertility showed high frequency in urban area than rural area, this agreed with study done in Basrah which found that the majority of infertility present in the center of Basrah⁽¹⁹⁾ & with study in south India which found the percentage of infertile females was more in urban than rural in the three study areas⁽²⁶⁾.

In this study the low frequency of contraceptive users was found in both groups (PCOS

infertility & the other causes of infertility groups) & this agrees with study in south India⁽²⁶⁾ in which infertile women in all the three studied districts used less number of contraceptives.

In the present study infertile women with PCOS presented as primary infertility (73.56%) & less frequently was secondary infertility. This agreed with study that done in Basrah which found about 61.8% of infertile women had primary infertility⁽²⁵⁾ & agreed with a study done in India in which primary infertility due to PCOS was 84.76%⁽¹⁷⁾, and with study in South India which indicated that primary infertility was more dominant than secondary infertility, the PCOS infertility is due to anovulation and this explain why most women present in primary infertility⁽²⁶⁾.

The duration of infertility (<5 years) was more in PCOS infertility than other causes of infertility, this agreed with study done by Cahill D J. in 2002⁽²⁷⁾, and with study in Basrah which found about 74% of cases had duration of infertility less than 5 years⁽²⁵⁾.

One of the metabolic changes in PCOS is diabetes mellitus, found in the present study as (2.29%), in an integrated health care delivery system in northern California, PCOS was associated with diabetes (OR 2.45, confidence interval 2.16–2.79), hypertension (OR 1.41, 1.31–1.51) and known dyslipidemia (OR 1.53, 1.39–1.68), even after adjusting for BMI and known confounders, they demonstrated that PCOS is independently associated with higher odds of major cardiovascular risk factors such as diabetes, hypertension, dyslipidemia, and obesity. These results support and extend previous studies that observed an association between PCOS and these risk factors that is independent of age and BMI in selected populations^(28, 29, 30). Only this may be explained by the fact that Diabetes mellitus (DM) is a late onset complication of

PCOS ,in the study done in Tikrit Teaching Hospital 23% of patients with PCOS has abnormal carbohydrate metabolism in form of fasting hyperglycemia & frequency of hyperglycemia more in obese than over weight & normal ⁽¹⁸⁾, in the study done in Chicago & other study in Pennsylvania the young women with PCOS had impaired glucose (35%,31% respectively)⁽³¹⁾ , the incidence of impaired glucose tolerance, type 2 diabetes mellitus, obesity, hypertension, and dyslipidemia, as well as of coronary and vascular disease may be higher in women with PCOS during their reproductive years than others ⁽³⁰⁾ .

The commonest clinical presentations of PCOS women in the present study are dysmenorrhea, irregular menstrual cycle, & oligomenorrhea, these results were similar to study in the University of Southern California, School of Medicine , Los Angeles⁽³²⁾ and a study in Kamal Al-Samarrae hospital⁽¹⁶⁾, but does not agree with study done in Unselected Caucasian Women from Spain & in the Greek Island of Lesbos ^(33, 34) which found the oligomenorrhea to be 19.5%,14.6% respectively .

Hirsutism which is one of the signs of hyperandrogenemia ,in the present study manifested in 82.7% of PCOS women ,nearly same findings were found by other studies in ^(33, 34, 32) which (70% & , 87.5%)of women diagnosed with PCOS demonstrated hirsutism,where as Tikrit study showed low rate (56.7,87.5) ⁽¹⁸⁾ .

The other sign of hyperandrogenemia in women with PCOS is acne ,which is manifested in the present study in 60.6% which is higher than the finding in study that done in Britain ,which described acne in 35% of patients with PCOS⁽¹⁴⁾ ,and was in unselected Caucasian Women from Spain & Tikrit Teaching Hospital ^(18, 20) ,which found acne (12.3%, 16.7% respectively) in patients with PCOS ,but this study agreed with study done in Canada ⁽³²⁾ which found that the prevalence of acne among PCOS was 69 % this may be explained by the differences in genetic and environmental factors, also the life style between the countries and the use of cosmetic agents that contain vitamins & antibiotic materials that prevent the occurrence of acne.

Galactorrhea is one of the signs that present in PCOS women it was found in the present study in 22.9% which is due to elevated serum level of prolactin this was higher than was found in Canada where galactorrhea was found in few patients 12%⁽³²⁾ .

In this study the hormonal profile showed elevated serum LH level 90.8% & normal level of FSH 86.2 % and increasing in FSH level just 5.74% so ,it means increase in LH/FSH ratio and agreed with the study done in Tikrit Teaching Hospital ⁽¹⁸⁾,which found high LH/FSH ratio(≥ 2) in 73% of PCOS and this coincides with study in Pennsylvania, which found elevated serum level of LH & low –to normal level of FSH in about 75%⁽³¹⁾, but not agreed with study done in India ⁽¹⁷⁾ which found 17.18% increase in LH level & LH/FSH ratio found (36%) in study done by John et al in 2005 ⁽³⁵⁾ .

There was also elevation in serum prolactin level in the present study in 52.87% this does not coincide with study done in India which found hyperprolactinemia is 11.49% of PCOS⁽³⁶⁾, and not agree with the study in Los Angeles who found hyperprolactinemia is 12% in PCOS ⁽³²⁾ .

CONCLUSION:

It was found that PCOS infertility comprises more than one fourth of causes of infertility among infertile women and PCOS was more among patient with primary infertility and young age group.

REFERENCES:

1. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. *Lancet*. 2007;370:685-97.
2. Cela E, Robertson C, Rush K .women with acne: hormone profiles and clinical findings. *J Pakistan Association of Dermatologists* 2010; 20: 194-98.
3. Sam S, Dunaif A Polycystic ovary syndrome: syndrome XX? *Trends Endocrinol Metab* 2003; 14:365–70.
4. Joan C. Lo, Seth L. Feigenbaum, Jingrong Yang, Alice R. Pressman, Joe V. Selby and Alan S. Epidemiology and Adverse Cardiovascular Risk Profile of Diagnosed Polycystic Ovary Syndrome. *J Clinical Endocrinology & Metabolism (JCEM)* 2006; 91: 1357.
5. Zacur HA. Epidemiology, clinical manifestations and pathophysiology of polycystic ovary syndrome. *Adv. Stud Med.* 2003;3 : S733-S739.
6. Boomsma CM, Fauser BC, Macklon NS. Pregnancy complications in women with polycystic ovary syndrome..*Semin. Reprod. Med.* 2008;26: 72–84.

7. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population. *J Clinical Endocrinology & Metabolism* June 2004;89:2745–49.
8. Palmert MR, Gordon CM, Kartashov AI, Legro RS, Emans SJ, Dunaif A. Screening for abnormal glucose tolerance in adolescents with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2002;87:1017–23.
9. Apridonidze T, Essah PA, Iuorno MJ, Nestler JE. Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2005; 90:1929–35.
10. Atiomo W, Khalid S, Parameshweran S, et al . Proteomic biomarkers for the diagnosis and risk stratification of polycystic ovary syndrome: a systematic review. *BJOG*, 2009;116:137–43.
11. Essah PA, Wickham EP 3rd, Nunley JR, Nestler JE. Dermatology of androgen-related disorders. *Clin Dermatol* 2006;24:289-98.
12. Shaw JC. Acne: Effect of hormones on pathogenesis and management. *Am J Clin Dermatol* 2002; 3: 571-78.
13. Homburg R. Polycystic ovary syndrome. *Best Pract Res Clin Obstet Gynaecol* 2008; 22: 261-74.
14. Balen A H . Secondary amenorrhea in Dewhurt's textbook of obstetric and Gynecology for postgraduates 7th edition , by D Keith Edmonds , 2007;Ch: 6:42-60.
15. Francisco Álvarez-Blasco,; José I. Botella-Carretero, ; José L. San Millán,; Héctor F. Escobar-Morreale. Prevalence and Characteristics of the Polycystic Ovary Syndrome in Overweight and Obese Women. *Arch InternMed.* 2006;166:2081-86.
16. Hussein SN. The prevalence of polycystic ovary syndrome among group of infertile women in Kamal Al-Samarae hospital ; thesis submitted to scientific council of community and family medicine .Iraqi Board for medical specialization in family medicine,supervised by Al-Warid N J& Abu Ragheif Z, 2004.
17. Lavanya R ,Deepika K, Madhuri P .Polycystic ovaries and infertility: Our experience. *J Human Reproductive Sciences* ,Jul –Dec 2008; 1: 65–72.
18. Eman A Dawood.Polycystic ovary syndrome in patients attending Tikrit Teaching Hospital; thesis submitted to scientific council of community and family medicine .Iraqi Board for medical specialization in family medicine, supervised by prof. Al-Sharbatti S. ,2007.
19. Fahimeh R T, Masoumeh S, Maryam T, et al . The prevalence of polycystic ovary syndrome in a community sample of Iranian population: Iranian PCOS prevalence study. *J Reproductive Biology and Endocrinology*2011,9:39.
20. Miryam A, Rosa M C , José L S, et al . A Prospective Study of the Prevalence of the Polycystic Ovary Syndrome in Unselected Caucasian Women from Spain. *J Clinical Endocrinology & Metabolism* July 2000;85 :2434.
21. Evanthia DK , Chryssa R K, Angeliki T B, et al . A Survey of the Polycystic Ovary Syndrome in the Greek Island of Lesbos: Hormonal and metabolic profile. *J Clinical Endocrinology & Metabolism*, Nov.1999;84:4006.
22. Abha M , Mark H , Siladitya B Effect of female age on the diagnostic categories of infertility. *Oxford J Medicine Human Reproduction* ,2007;23:538-42.
23. Lavanya R , Deepika K, Madhuri P .Polycystic ovaries and infertility: Our experience. *J Human Reproductive Sciences* ,Jul –Dec. 2008;1: 65–72.
24. Abha M , Mark H , Siladitya B Effect of female age on the diagnostic categories of infertility. *Oxford J Medicine Human Reproduction* ,2007,23:538-42.
25. Abdul-Kader RA.Female infertility :A studyt on risk factors ; thesis submitted to scientific council of community and family medicine .Iraqi Board for medical specialization in family medicine,supervised by Ajeel NA,2008.
26. Shamila S , Sasikala SL. Primary Report on the Risk Factors Affecting Female Infertility in South Indian Districts of Tamil Nadu and Kerala. *Indian J of Community Medicine*, Jan-Mar 2011;36: 59–61.

POLYCYSTIC OVARIAN SYNDROME

27. Lo, J C, Feigenbaum, S L, Yang, J, Pressman A R, Selby J V and Go A S. Epidemiology and Adverse Cardiovascular Risk Profile of Diagnosed Polycystic Ovary Syndrome. *J Endocrinology & Metabolism (JCEM)* 2006;91:1357-63.
28. Apridonidze T, Essah PA, Iuorno MJ, Nestler JE. Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2005;90:1929–35.
29. Talbott EO, Zborowski JV, Rager JR, Boudreaux MY, Edmundowicz DA, Guzick DS. Evidence for an association between metabolic cardiovascular syndrome and coronary and aortic calcification among women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2004 ; 89:5454–61.
30. Carolyn J A, Edward P T, and Norman E L. Polycystic Ovary Syndrome: A Major Unrecognized Cardiovascular Risk Factor in Women. *J Reviews in Obstetrics Gynecology*, 2009; 2: 232–39.
31. Legro R S. polycystic ovary syndrome: Current and future treatment paradigms. *Am. J. Obstet. Gynecol.*, 1998;179:S101-8.
32. Carmina E, Lobo R A. Hirsutism, Alopecia, and Acne, In: principles and practice of Endocrinology and Metabolism. 1,3rd edition, by Kenneth L. Becker., 2001, Ch.101:991-1008.
33. Ricardo A, Keslie S W, Rosario R, et al. The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population. *J Clinical Endocrinology & Metabolism*, June 2004; 89: 2745-49.
34. Brooke R, Sara S, Jennifer D, et al. Prevalence of Metabolic Syndrome and Related Characteristics in Obese Adolescents with and without Polycystic Ovary Syndrome. *J Clinical Endocrinology & Metabolism*, December 2008, 93: 4780–86.
35. John C M, William S Y, Juanita H, et al. The effects of a low-carbohydrate, ketogenic diet on the polycystic ovary syndrome: A pilot study. *The Journal of Nutrition & Metabolism*, 2005;2: 35.
36. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA*, 2006, 295:1549–55.