Maternal polycystic ovary syndrome (PCOS) and Antenatal (ANC) Complications: A Case Control Study

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Abstract— *Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women. Evidences shows variable finding regarding it's effect on pregnancy outcomes. This present study was conducted to determine whether maternal polycystic ovary syndrome (PCOS) is associated with adverse pregnancy outcomes in antenatal period. Prospective observational study, carried out in the department of Obstetrics and Gynecology, Indraprastha Apollo Hospitals, New Delhi, including 64 women with PCOS and 64 normal pregnant women between January 2013 and November 2014. It was found that Gestational diabetes mellitus (GDM) was significantly more frequent in the PCOS group than in the control group (p value = 0.009; OR=2.698 (1.213-6.001), this difference was not found statistically significant. Pregnancy induced hypertension (PIH) was also found significantly more frequent in the PCOS group than in the control group (p value=0.014; OR=3.41 (1.176-9.885). Miscarriage rate was not significantly different among two groups. So it can be concluded that women affected by PCOS carry an increased risk of adverse pregnancy outcomes specially GDM and PIH.*

Key word: Polycystic ovary syndrome (PCOS), ANC Complications, GDM, PIH.

I. INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women, with prevalence as high as 15% when the broader Rotterdam Criteria are applied.[1] Despite its prevalence, PCOS is a disease with an unclear cause, varying diagnostic criteria, expansive clinical effects, and debatable management.

As per Rotterdam criteria[2] PCOS is characterized by presence of any two out of these three criterias i.e. Oligo/amenorrhea, Clinical or laboratory evidence of hyperandrogenemia and Ultrasound imaging of polycystic ovaries (either 12 or more follicles measuring 2-9 mm in diameter or increased ovarian volume (>10cm^3).

In non pregnant women, PCOS is known to be associated with menstrual irregularities, decreased fertility, insulin resistance, diabetes mellitus, and hyperandrogenism.[3] For this population to become pregnant, many women require assisted reproductive techniques in addition to the medical treatment of insulin insensitivity.[4-6].Once this previously sub fertile population becomes pregnant, the effect of maternal insulin insensitivity and hyperandrogenism on the fetus must be considered.

Hyperandrogenism and insulin resistance from the metabolic hallmark of PCOS women. Several studies in diverse populations of PCOS women have demonstrated an increased risk of hyperinsulinemia,[7] insulin resistance, dyslipidemia,[8,9] glucose intolerance,[10] hypertension[7] and metabolic syndrome.[11] A

significant section of lean PCOS women have baseline intrinsic insulin resistance. Over 50% of women with PCOS are either overweight or obese further modifying this metabolic phenotype.[12] Because those with superimposed obesity have additional insulin resistance contributed by the excess adipose tissue. And it has been recently reported that obesity itself is associated with adverse reproductive and obstetric outcomes.[13] The baseline insulin resistance seems to be exacerbated with entry into pregnancy. The metabolic risks of PCOS may therefore adversely affect both maternal and fetal status, potentially leading to an increased manifestation of complications such as increased incidence of spontaneous miscarriage, Gestational diabetes mellitus (GDM), Pregnancy induced hypertension (PIH) and pre-eclampsia etc.

So this study was conducted on pregnant women to find out the antenatal complications associated with PCOS.

II. METHODOLOGY

A case control observational study was conducted on 128 in the Department of Obstetrics and Gynecology and center for Fetal Medicine, Indraprastha Apollo hospitals; New Delhi from January 2013 to November 2014 after being approved by institutional Ethical committee.

For this study after taking informed written consent 128 pregnant women (64 in each group i.e. PCOS vs non PCOS pregnant women) from obstetrics and Gynecology clinic were recruited. For this all those previously diagnosed cases of Polycystic Ovarian Syndrome, who conceived either spontaneously or through Artificial Reproductive Technology(ART) and who gave consent to be part of study were recruited for study group. For control group age matched pregnant women were taken. Women having any disease were excluded from this study.

Based on Rotterdam consensus criteria, women were considered to have PCOS, if she met at least 2 of the following criteria (prior to conception):-

1. Oligomenorrhoea (menstrual cycle longer than 35 days).
2. Clinical or biochemical evidence of hyperandrogenism such as high tonic LH , increased testosterone, DHEAS level or hyperinsulinemia, hirsutism, acne, obesity(at values greater than reference range).
3. Typical morphology of polycystic ovaries on ultrasound scans

All enrolled women were interviewed about detailed menstrual history, obstetric history and medical history and then these women examined. Observations were recorded in semistructured performa. All these women were followed throughout the pregnancy and outcomes were also recorded and analysed.

At First prenatal visit along with routine antenatal tests ,Measurement of fasting blood glucose, HbA1C, or random blood glucose was done on all women.GDM was diagnosed ,If fasting plasma glucose was > 92 mg/dl but <126 mg/dl. 75-g Oral Glucose ToleranceTest(OGTT) was done at 24-28 weeks if fasting plasma glucose was < 92 mg/dl. GDM was diagnosed if One or more of the following values from a 75-g OGTT equaled or exceeded:-Fasting Plasma Glucose >92mg/dl, 1-h plasma glucose>180mg/dl or 2-h plasma glucose> 153mg/dl.

PIH was defined as hypertension with a systolic blood pressure over 140 mm Hg or diastolic blood pressure over 90 mm Hg, with or without proteinuria, developing after 20 weeks of gestation

Data thus obtained was analyzed using SPSS version 16. Proportions were expressed in percentage and analyzed using chi-square test. T-test was used for comparing the means of two groups for normal distribution. Odd's ratio was used to find out strength of association.

III. RESULTS

In present study total 128 pregnant (PCOS (n=64) and normal (n=64)) women were recruited and followed throughout pregnancy till delivery. Both group were comparable as per age and BMI. (Figure 1& 2)

Figure 1

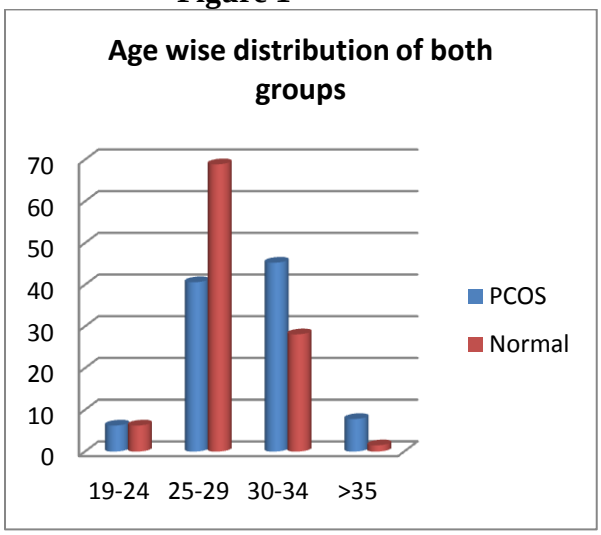
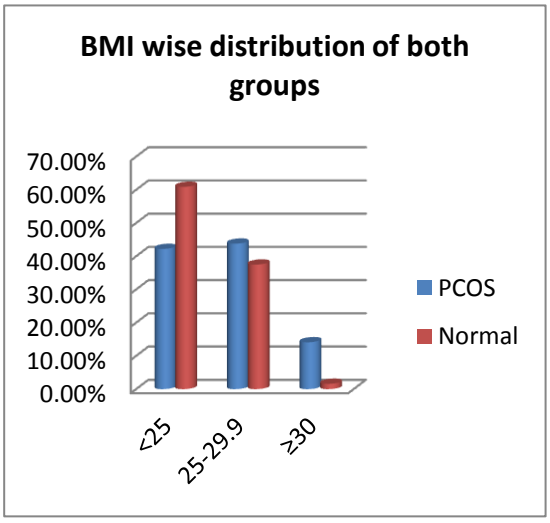


Figure 2



When proportion of pregnant women with history of miscarriage were compared between PCOS and normal pregnant women it was observed that in PCOS group 18 (28%) women had ≥1 miscarriage while in normal pregnant women group 16(25%) women had history of miscarriage. This variation was not found significant (p>0.05). (Table 1)

Table 1
Comparison of history of miscarriage among PCOS and normal pregnant women

S. No.	H/o Miscarriage	PCOS (N=64) No. (%)	Normal (N=64) No. (%)	*P Value	Odds Ratio (95% CI)
1	0	46 (72%)	48 (75%)	0.689	1.125 (0.631-2.004)
2	≥1	18 (28 %)	16 (25%)		

Chi square test

When proportion of women with GDM were compared between PCOS and normal pregnant women, 18 (29.5%) had GDM while in normal pregnant women 7 (11%) had history of GDM respectively. GDM was found significantly more in pregnant women with PCOS (p<0.05). (Table 2)

Table 2
Comparison of Proportion of pregnant women with GDM in PCOS and normal pregnant

S. No.	GDM	PCOS (N=61) No. (%)	Normal (N=64) No. (%)	*P Value	Odds Ratio (95% CI)
1	No	43 (70.5%)	57 (89%)	0.009	2.689 (1.213-6.001)
2	Yes	18 (29.5 %)	7 (11%)		

Chi square test

Likewise the GDM, PIH also was found 3.41 times more in PCOS group than normal pregnant women group i.e. 21.3% and 6.2%) respectively. This variation was found significantly ($p<0.05$). (Table 3) dl.

Table 3
Comparison of Proportion of pregnant women with PIH in PCOS and normal pregnant

S. No.	PIH	PCOS (N=61) No. (%)	Normal (N=64) No. (%)	*P Value	Odds Ratio (95% CI)
1	No	48 (78.7%)	60 (93.8%)	0.014	3.41 (1.176-9.885)
2	Yes	13 (21.3 %)	4 (6.2%)		

**** Chi square test***

IV. DISCUSSION

The present study was carried out in Indraprastha Apollo hospital with the aim of studying complications during pregnancy in cases of PCOS (Risk of miscarriages, Risk of Gestational diabetes mellitus (GDM) and Pregnancy induced hypertension) compared with normal healthy pregnant women. This was a prospective observational study. The study was conducted on 128 subjects from January 2013 to November 2014.

In this study, mean age of PCOS group was 29.88 ± 2.88 (Range: 24-35) years and mean age of control group was 28.45 ± 2.976 (Range: 19-35) years. Other studies[50] done on complications during pregnancy had almost similar mean age. The study on 93 women with PCOS and 73 controls conducted by Stefano Palomba et al in 2010 showed mean age distribution among PCOS group as 30 years and among control group as 30 years.[14]

In present study miscarriage rate was found 28% that was almost quite similar to other authors[15,16] This proportion was not significantly high in PCOS group as compared to normal population. Our study is supported by the previous data from a meta-analysis of nine studies by Heijnen EM et al that reported no significant difference in miscarriage rates between PCOS and non-PCOS patients after IVF (random effects OR 1.0; 95% CI 0.5 to 1.8).[17] The current literature indicates that, regardless of the method of conception, miscarriage risk is related to obesity rather than PCOS or any other cause of infertility. This fact was supported by Maheshwari A et al found that, In IVF conceived pregnancies, women with a BMI ≥ 30 had a higher risk of miscarriage compared to women with a BMI < 30 (OR 1.53, 95% CI 1.27-1.84 ($p <0.001$).[9]

In present study GDM was found in 29.5% of PCOS pregnant women which was similar to other authors[18] Normal pregnancy itself induces an insulin resistant state and insulin resistance is thought to be the etiology of PCOS. Therefore, many studies have suggested that women with PCOS are likely to develop GDM. In this study also proportion women with GDM was found to be significantly higher in PCOS group as compared to normal pregnant women. Our results were similar to those reported by Enrique Reyes-Munoz et al who confirmed that there is an increased risk of GDM in Mexican women with a history of infertility and PCOS. However results of this study were controlled for age, pre-gestational BMI and parity.[19] Our results were also similar to those reported by Yunhui Wang et al, whose results indicated that the "typical PCOS" with obesity and the lean phenotype of PCOS are both risk factors for GDM. They also suggested that obesity may also play a role in the development of GDM.[20] Thus we suggest that PCOS itself is a risk factor for GDM but associated obesity may also contribute to GDM.

In our study, there was statistically significant higher proportion of PIH among PCOS group as compared to normal pregnant women. Our findings were similar to Meta analysis by Boomsma CM et al and Lucinda E et al, who found significantly higher incidence of PIH in PCOS women.[21,22] Our findings were also consistent with Yunhui Wang et al, [20] who found that PCOS patients have a greater risk of pregnancy-induced hypertension in pregnant women compared with controls. This indicated that PCOS is an independent risk factor for development of PIH. This increased risk may be due to its associated insulin resistance or it may also be due to hyperandogenic and chronic inflammatory pathology.

V. CONCLUSION

Pregnant Indian women with a history of PCOS are at increased risk for developing GDM and PIH, but they are not at increased risk of miscarriage. These complications are more likely to occur in obese women with PCOS. These results, Obtained from a small sample of PCOS women, are in accordance with growing evidence that PCOS may be associated to a higher prevalence of adverse pregnancy outcomes. These findings warrant counseling of women with PCOS especially prior to IVF on the potential benefits of weight loss prior to pregnancy. These women may need increased surveillance during pregnancy and parturition.

CONFLICT

None declared till date.

REFERENCES

[1] The Amsterdam ESHRE/ASRM-Sponsored third PCOS Consensus Workshop Group. Fertility Sterility. 2012 January; Vol. 97: No. 1

[2] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2004) Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19(1):41–47)

[3] American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 108: polycystic ovary syndrome. Obstet Gynecol 2009;114:936-49.

[4] Azziz R, Ehrmann D, Legro RS, et al, Troglitazone improves ovulation and hirsutism in the polycystic ovary syndrome: a multicenter, double- blind, placebo-controlled trial. PCOS/Troglitazone study group. J Clin Endocrinol Metab 2001;86:1626-32.

[5] Lord JM, Flight IH, Norman RJ,Metformin in polycystic ovary syndrome: systematic review and meta-analysis, BMJ 2003;327:951-3.

[6] Heijnen E, Eijkemans M, Hughes E, Laven J, Macklon N, Fauser B,A meta-analysis of outcomes of conventional IVF in women with polycystic ovary syndrome. Hum Reprod Update 2006;12:13-21.

[7] Ehrmann DA, Wild RA, Painter PC, Coulson PB. Polycystic ovary syndrome. N Engl J Med . . . . 2005 Mar .24;352(12):1223-36.012,

[8] SimonaFica, Alice Alb, Madalina Constantin,GeorgianaAlinaDobri. Insulin resistance and fertility in polycystic ovary syndrome. Journal of Medicine and Life. 2008 October-December; Vol 1: No.4,

[9] Legro RS, Castracane VD, Kauffman RP. Detecting insulin resistance in polycystic ovary syndrome: purposes and pitfalls.ObstetGynecolSurv 2004; 59:141–54.

[10] Ehrmann DA, Barnes RB Rosenfield RL, CavaghanMK,Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes Care. 1999 Jan; 22(1):141-6.

[11] Dokras A, Bochner M, HollinrakeE, Markham S, Vanvoorhis B, Jagasia DH. Screening women with polycystic ovary syndrome for metabolic syndrome.Obstet Gynecol. 2005 Jul; 106(1):131

[12] Carmina E, Legro RS, StametsK, Lowell J, Lobo RA. Difference in body weight between American and Italian women with polycystic ovary syndrome: influence of the diet. Hum Reprod. 2003 Nov; 18(11):2289-93.

[13] Dokras A, Baredziak L, Blaine J, Syrop C, VanVoorhis BJ, Sparks A.Obstetric outcomes after in vitro fertilization in obese and morbidly obese women. Obstet Gynecol. 2006 Jul;108(1):61-9.

[14] Stefano Palomba, Angela Falbo, Tiziana, Russo, AchilleTolino, Francesco Orio, and FulvioZullo Pregnancy in women with polycystic ovary syndrome: the effect of different phenotypes and features on obstetric and neonatal outcomes. Fertility and Sterility. 2010 October;Vol. 94:No. 5.

[15] Jakubowicz DJ, Iuorno MJ, Jakubowicz S, Roberts KA, Nestler JE. Effects of metformin on early pregnancy loss in the polycystic ovary syndrome. J Clin Endocrinol Metab. 2002;87:524–9.

[16] Gray RH, Wu LY. Subfertility and risk of spontaneous abortion. Am J Public Health. 2000;90:1452–4.

[17] The World Health Organization Western Pacific Region. The international Association for the Study of Obesity, and The international Force. The Asia-Pacific perspective: redefining obesity and its treatment. Sydney: Health Communications Australia Pty Limited; 2000

[18] Veltman-Verhulst SM, van Haeften TW, Eijkemans MJC, de Valk HW, Fauser BC, Goverde AJ. Sex hormone-binding globulin concentrations before conception as a predictor for gestational diabetes in women with polycystic ovary syndrome. Hum Reprod. 2010;25:3123–8. [PubMed: 20943702]

[19] Enrique Reyes-Munoz, a Guillermo Castellanos-Barroso,Brenda Y. Ramírez-Eugenio,Carlos Ortega-Gonzalez, Adalberto Parra, Alfredo Castillo-Mora, and Julio F. De la Jara-Díaz.The risk of gestational diabetes mellitus among Mexican women with a history of infertility and polycystic ovary syndrome.FertilSteril.2012;97:1467–71.

[20] Liao AW, Heath V, Kametas N, Spencer K, Nicolaides KH. 2001.First-trimester screening for trisomy 21 in singleton pregnancies achieved by assisted reproduction. *Hum Reprod* **16**(7): 1501–1504

[21] C.M.Boomsma, M.J.C.Eijkemans E.G. Hughes, G.H.A.Visser, B.C.J.M.Fauser and N.S.Macklon. meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. Human Reproduction Update. 2006; Vol.12:No.6 pp. 673–683.

[22] Simon Kayemba-kays,Catherine Peters, Michael P.P. Geary, Nathan R. Hill, David R. Mathews,Peter C. hind marsh. Maternal Hyperinsulinism and Glycaemic Status in the First Trimester of Pregnancy are Associated with the Development of Pregnancy Induced Hypertension and Gestational Diabetes. 14 December 2012 as Manuscript EJE-12-0609.