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To evaluate the risk of GDM in antenatal mothers with previous history of PCOS

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Abstract

Background: The main objective of the study is to evaluate the risk and pregnancy outcomes of Gestational Diabetes mellitus in women with previous history of Polycystic Ovarian Syndrome as compared to antenatal women without previous history.

Methods: This is a case-control (observational) study conducted in Government Chengalpattu Medical College and Hospital, Chengalpattu in Obstetrics and Gynecology department, Tamil Nadu. All antenatal women attending the outpatient or labour room with Polycystic Ovarian Syndrome who satisfy the criteria were included and studied for development of gestational diabetes, pregnancy outcomes, associated conditions as compared to antenatal women without previous history of Polycystic Ovarian Syndrome.

Results: Out of 112 in our study population, 56 belonged to antenatal women with Polycystic Ovarian Syndrome and 56 belonged to normal pregnant women. In this study, about 42% of the Polycystic group developed Gestational Diabetes which is statistically significant as compared to 12.5% in normal pregnant group. Among the Polycystic group, 67% had conceived spontaneously, while 88% in normal group had spontaneous conception. Among the Polycystic group, 16% conceived by Artificially Reproductive Technique which is statistically significant, while 7% in normal group have conceived through Artificial Reproductive Technique. While studying the maternal outcome in the Polycystic Ovary group, 48% had vaginal delivery, 14% had assisted vaginal delivery and 37.5% had Caesarean births. Among normal group, 62% had vaginal delivery, 9% has Assisted Vaginal Delivery, 28% had Caesarean births.

Conclusion: Gestational Diabetes mellitus and Polycystic Ovarian Syndrome are the emerging diseases that not only affects the quality of life of the patients but also have genetic influences that carry over to the next generations and hence appropriate diagnosis and treatment are necessary.

Keywords: GDM-Gestational Diabetes Mellitus, PCOS-Polycystic Ovarian Syndrome, Infertility, ART-Artificial Reproductive Technique

Introduction

Gestational diabetes mellitus is defined as carbohydrate intolerance of variable severity with its onset or first recognition during pregnancy [ACOG 2013]. The incidence of Gestational Diabetes mellitus has increased approximately from 6.0% in 2016 to 8.3% in 2021 [1].

As pregnancy progresses, insulin resistance increases due to hormones secreted by placenta which in turn requires a compensatory increase in insulin secretion. Advancing age and increased BMI are potential risk factors for developing GDM. Women with GDM further develop overt diabetes in the following 20 years.

Babies born to GDM mothers are also more prone to develop obesity and diabetes in their future. Thus, it becomes a continuous cycle of transmitting glucose intolerance from one generation to another [20].

Government of India has considered GDM as an important public health problem and has issued guidelines to address the need of high prevalence of GDM in India. Services are provided under Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA). All antenatal women and GDM mothers should visit the facility on PMSMA day for the diagnosis and management of GDM according to the guidelines. It is essential that all opportunities and channels of communications be leveraged to promote delivery of GDM services for continuum of care to both mother and the child.

PCOS is the most common endocrine disorder with an incidence of 3% to 22.5% in India [9, 10]. It is the most common cause of hyperandrogenism, hirsutism and anovulatory cause of infertility in the developed countries and insulin resistance plays a major role.

This reproductive endocrine disorder is lifelong, characterized by amenorrhoea, oligomenorrhoea from puberty with acne and hirsutism arising in the teens ^[16]. Insulin resistance is a condition in which the cells remain hypo responsive to insulin.

PCOS women have several pregnancy complications like preeclampsia, preterm labour, spontaneous abortion, in addition to gestational diabetes mellitus. It has a good hereditary basis requiring a multidisciplinary approach to treatment ^[4]. PCOS women have greater risk of development of endometrial cancers and other cardio-vascular issues. They are also a high-risk group for metabolic syndrome, and they must be screened earlier to prevent complications from the syndrome. Infertility is also a major cumbersome issue related to PCOS. This can also be related to changing food habits and lifestyle. These are the modifiable risk factors. Creating awareness among the public is the best option available.

The increased prevalence and the shared metabolic similarities between Polycystic Ovarian Syndrome and Gestational Diabetes Mellitus lead us to investigate the risk factors, maternal and fetal outcome from our study. We can help minimise the risk associated with diabetes in pregnancy by identifying the PCOS patients and screening them beforehand. Also, to increase the awareness regarding the risks associated with diabetes during the pre-pregnancy counselling.

Materials and Methods

Antenatal patients attending OPD or admitted in labour ward with PCOS who satisfy the inclusion and exclusion criteria were included till the sample size (n=112) is reached and compared to equal number of normal pregnant women without PCOS around 20 weeks of gestation and followed up till delivery.

This study was carried out in Government Chengalpattu Medical College and Hospital, Chengalpattu from March 2020 to March 2021.

Inclusion criteria

1. Antenatal mothers with clinical features of PCOS
2. History of primary infertility
3. BMI > 30 Kg/m²
4. USG suggesting appearance of polycystic ovaries-
 - Presence of 12 or more follicles, 2-9 mm in diameter in either ovary.
 - Increased ovarian volume > 10 ml (on the basis of Rotterdam's criteria-Menstrual irregularities, Clinical or biochemical hyperandrogenism, USG showing appearance of polycystic ovaries).

Exclusion Criteria

- Patients with known Type 1 and type 2 diabetes mellitus.
- Cushing's syndrome

Detailed history regarding the symptoms, diagnosis, and management of previous PCOS were elicited. General examination and features of thyroid abnormalities, hyperandrogenism like acne, hirsutism, insulin resistance if any are documented. History regarding infertility, treatment for infertility, mode of conception, previous history of GDM, anomalous baby, recurrent abortion, and history of LGA babies, GHT, IUD, H/O DM in families were elicited.

56 Patients with such positive history are included in the study as the PCOS group.

56 more antenatal patients with no such previous evidence or history of PCOS are included in the normal or control group. Both these groups undergo OGCT for the diagnosis of GDM and

are followed till delivery for analysing the risk, outcomes, and association with other condition. Oral Glucose Challenge Test (OGCT) was used to diagnose Gestational Diabetes mellitus according to DIPSI (Diabetes In Pregnancy Study Group India) criteria ^[5].

The patient was asked to drink 75 grams of glucose mixed with 300ml of water and 2 ml of venous blood was withdrawn after 2 hours irrespective of overnight fasting status ^[20].

The threshold plasma level of > or = to 140mg/dl is taken as cut-off for GDM.

OGCT is repeated in second and third trimester. Patients who have OGCT value > 140 are labelled as GDM and are treated with Medical Nutritional Therapy, Metformin and Insulin.

Pregnant women with controlled plasma glucose, induction of labour was planned at or after 39 weeks of pregnancy.

In pregnant women with poor glycaemic control or those with associated complications like hypertensive disorder of pregnancy, previous history of still birth and other complications should be delivered earlier at around 38 completed weeks. Vaginal delivery was preferred over LSCS.

The outcomes and risk associated with GDM are studied.

For Quantitative outcome, the association between the variables and their quantitative outcome was assessed by comparing the mean values and their mean differences and 95% Confidence Interval were presented.

Independent t test was used to find the statistical significance.

For Categorical outcome, the association between explanatory variables and categorical outcome was assessed by finding odd's ratio and comparing the percentages.

Odd's ratio and 95% CI is presented.

Chi square is used to test the significance.

P Value < 0.05 was considered statistically significant.

Results

Our study was a case-control study with a sample size of 112 patients with 56 in each group. One group of 56, with previous history of PCOS diagnosed and the other group had no PCOS previously. Both the groups were followed for development of Gestational Diabetes Mellitus and the results analysed. In our study, we have followed DIPSI criteria for diagnosing GDM and Rotterdam criteria for diagnosing PCOS. Among the PCOS group, 42% had GDM, while 12% in normal group had GDM with a significant 'p' value (0.0006). This shows an increased incidence of GDM in PCOS pregnant women. (Table 1)

In the PCOS group, 16% were on MNT, 10% on OHA, 16% were treated with Insulin, whereas in the normal pregnant women, 5% were on MNT and 3% were on OHA and 3% on Insulin (Table 2).

In our study, acne was found in 19.6%, irregular cycles in 35%, scan finding suggestive of PCOS in 85.7%, hirsutism in 16% and acanthosis nigricans in 21% of PCOS group. In the normal group, acne was found in 5%, irregular cycles in 8%, hirsutism in 5% and acanthosis nigricans in 3% individuals. Their respective odd's ratio and 'p' value are enlisted below (Table 4).

Among the PCOS group, 16% have conceived by ovulation induction, while 7% in normal group have conceived through ovulation induction.

In the PCOS group, 16% have conceived by ART-IVF/IUI, while 5.3% in normal group have conceived through ART-IVF/IUI (Table 5).

Odd's ratio for infertility is 3.315 and hence PCOS is associated with higher infertility rates (p value 0.0155).

Among the PCOS group, 21% have family history of diabetes while 10% in normal group have associated family history of

DM. PCOS has association with diabetic family history (Odd's Ratio 2.27). 17.8% of PCOS pregnant women had hypothyroidism and among the PCOS group, 16% had GHT while only 3.57% in normal group had associated GHT. (Table 6). Patients with PCOS have association with GHT ('p' value 0.041). While comparing the maternal outcomes, in the PCOS group, 48% had NVD, 14% has Assisted Vaginal Delivery and 37.5% had Caesarean births (Table 7). Among normal group, 62% had NVD, 8.9% has Assisted

Vaginal Delivery, 28% had Caesarean births. Babies born to GDM mothers with prior history of PCOS have had higher rates of caesarean section than Normal pregnant women. While comparing the fetal outcomes, among PCOS group, 3.5% were still born, 21% had NICU admission, 75% were well babies. Among normal group, 1.7% were still born, 10% had NICU admission and 87% were well babies. Babies born to GDM mothers with prior history of PCOS have had higher rates of NICU admission than Normal pregnant women (Table 8).

Table 1: Elevated OGCT (Diagnosed as GDM) in PCOS vs Normal group

| Parameters | PCOS (n=56) | Normal (n=56) | Odd's Ratio | 95% Confidence Interval | 'p' Value |
|----------------------------------|-------------|---------------|-------------|-------------------------|----------------------|
| OGCT Elevated (Diagnosed as GDM) | 24 (42%) | 7 (12.5%) | 5.25 | 2.0253 to 13.6094 | 0.0006 (Significant) |

OGCT -Oral Glucose Challenge Test, PCOS-Poly Cystic Ovarian Syndrome

Table 2: Different treatment options in PCOS vs Normal group

| Treatment | PCOS (n=56) | Normal (n=56) |
|-----------|-------------|---------------|
| MNT | 9 (16%) | 3 (5%) |
| OHA | 6 (10.7) | 2 (3%) |
| Insulin | 9 (16%) | 2 (3%) |

MNT- Medical Nutrition Therapy, OHA – Oral Hypoglycaemic Agent

Table 3: Complications of GDM in PCOS vs Normal group

| Complications | PCOS(n=56) | Normal(n=56) | Odd's Ratio | 95% Confidence Interval | 'p' Value |
|-----------------------|------------|--------------|-------------|-------------------------|-----------|
| Polyhydraminos | 15 (26%) | 2 (3.5%) | 9.87 | 2.13 to 45.63 | 0.0034 |
| Anomalous baby | 5 (8.9%) | 1 (1.7%) | 5.39 | 0.60 to 47.73 | 0.1299 |
| Preterm birth | 6 (10.7%) | 3 (5%) | 2.12 | 0.50 to 8.93 | 0.3060 |
| Big baby (Wt > 4 Kgs) | 8 (14.2%) | 1 (1.7%) | 9.16 | 1.10 to 75.96 | 0.0400 |

Table 4: Comparison of features of PCOS seen in PCOS group vs Normal group

| Findings | PCOS (n=56) | Normal (n=56) | Odd's Ratio | 95% Confidence Interval | 'p' Value |
|----------------------|-------------|---------------|-------------|-------------------------|-----------|
| Acne | 11 (19.6%) | 3 (5%) | 4.319 | 1.13 to 16.44 | 0.032 |
| Irregular Periods | 20 (35%) | 5 (8%) | 5.666 | 1.94 to 16.50 | 0.001 |
| Hirsutism | 9 (16%) | 3 (5%) | 3.383 | 0.86 to 13.23 | 0.080 |
| Acanthosis nigricans | 12 (21%) | 2 (3%) | 7.36 | 1.56 to 34.65 | 0.011 |

Table 5: Mode of Conception in PCOS vs Normal group

| Mode of Conception | PCOS (n=56) | Normal (n=56) |
|------------------------|-------------|---------------|
| Spontaneous Conception | 38 (67%) | 49 (87.5%) |
| Ovulation Induction | 9 (16%) | 4 (7.1%) |
| IUI/IVF | 9 (16%) | 3 (5.3%) |

IUI – Intra Uterine Insemination, IVF – *In vitro* Fertilisation

Table 6: Association of various conditions with GDM in PCOS vs Normal group

| Associated Condition | PCOS (n=56) | Normal (n=56) | Odd's Ratio | 95% Confidence Interval | 'p' VALUE |
|-------------------------------------|-------------|---------------|-------------|-------------------------|-----------|
| GHT | 9 (16%) | 2 (3.57%) | 5.170 | 1.063 to 25.13 | 0.041 |
| Hypothyroid | 10 (17.8%) | 2 (3.57%) | 5.869 | 1.22 to 28.16 | 0.027 |
| Obesity (BMI>30 Kg/m ²) | 15 (26.7%) | 3 (5%) | 6.463 | 1.75 to 23.83 | 0.005 |
| Infertility | 17 (30%) | 6 (10.7%) | 3.632 | 1.30 to 10.07 | 0.013 |

GHT – Gestational Hyper-Tension, BMI – Body Mass Index, GDM – Gestational Diabetes Mellitus

Table 7: Mode of delivery in PCOS vs Normal group

| Mode of Delivery | PCOS (n=56) | Normal (n=56) |
|---------------------------|-------------|---------------|
| Normal Vaginal Delivery | 27 (48%) | 35 (62%) |
| Assisted Vaginal Delivery | 8 (14%) | 5 (8.9%) |
| Cesarean Delivery | 21 (37.5%) | 16 (28%) |

Table 8: Fetal Outcome in PCOS vs Normal group

| Fetal Outcome | PCOS (n=56) | Normal (n=56) |
|-------------------------|-------------|---------------|
| Well baby | 42 (75%) | 49 (87.5%) |
| NICU admission at birth | 12 (21.4) | 6 (10.7%) |
| Still born | 2 (3.57%) | 1 (1.7%) |

NICU – Neonatal Intensive Care Unit

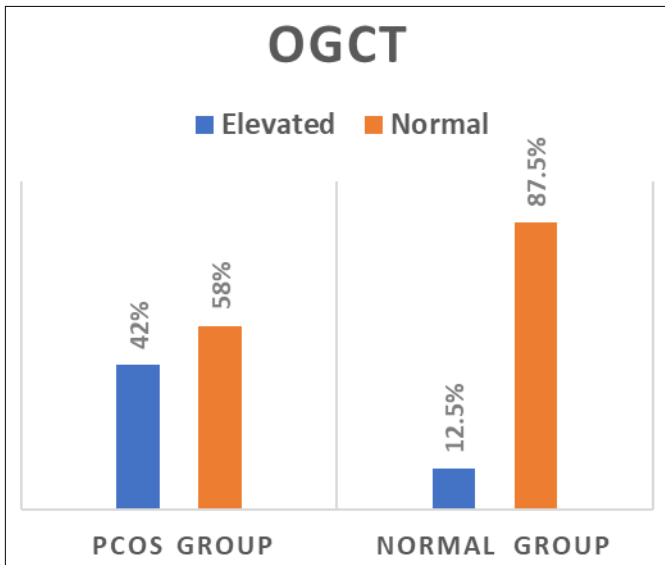


Fig 1: Association of group with cumulative OGCT levels in study population

Discussions

Out of 112 of our study population, 56 were PCOS pregnant women and 56 were normal pregnant women. In our study we have followed DIPSI criteria for diagnosing GDM and Rotterdam criteria for diagnosing PCOS. Our study has shown an increased rate of development of GDM in PCOS pregnant women as compared to normal pregnant women. In a study the prevalence of GDM was found to be 17.9% in Tamil Nadu (WHO criteria). The incidence of Gestational Diabetes mellitus has increased approximately from 6.0% in 2016 to 8.3% in 2021 [1].

In our study 42% of the 'PCOS' pregnant women developed GDM while 12.5 % of the 'normal' pregnant women developed GDM which is statistically significant (p value 0.0006). As we compare many studies, our study has showed an increased association of GDM in PCOS pregnant women thus proving that PCOS itself a significant risk factor for developing GDM. This is the key finding of our study. To validate our finding, a meta-analysis showed that women with PCOS have an elevated risk of GDM compared to women without PCOS [2, 3]. Also, another study has indicated an elevated risk of GDM in PCOS patients in both retrospective and prospective studies.

In a study, "Obstetric complications in women with polycystic ovary syndrome: a systematic review and meta-analysis" the meta-analysis shows that women with PCOS have shown significantly elevated risk of gestational diabetes mellitus, pregnancy-induced hypertension, preeclampsia, premature delivery, preterm, caesarean section rate, admission to an NICU pregnancy as compared with their controls [4].

Associated complications like pre-eclampsia and hypothyroidism are high in PCOS pregnant women compared to normal pregnant population. Our study has shown that there is an increased incidence of GHT in PCOS pregnant women compared to normal pregnant women. 16% of PCOS pregnant women developed GHT. Studies suggested that gestational hypertension and pre-eclampsia were found to be an accompanying co-morbidity in pregnancies complicated with GDM, and the possibility of recurrence in subsequent pregnancies in mothers prior to GDM [3, 4, 8, 11].

One of the complications of GDM per se is it has effects on the fetus too. Neonates born to GDM mothers are at risk of macrosomia, metabolic, hematological disorders, malformation,

risk of still birth and intra-uterine death. This is supported by a study, "What neonatal complications should the paediatrician be aware of in case of maternal gestational diabetes?" [6, 17].

In our study, 26% in PCOS Group had polyhydramnios, 8.9% had anomalous babies, 10.7% had preterm birth and 14.2% had big baby. In the normal group 3.5% had polyhydramnios, 2% had anomalous babies, 5% had preterm birth and 2% had big babies. Perinatal death, malformations and prematurity are mainly influenced by maternal glucose levels. Thus, knowing the risk factors to screen the disease priorly can prevent such complications [17].

5 % of normal pregnant women and 16% of PCOS pregnant women were on meal plan while 16 % of PCOS pregnant women and 3 % of normal pregnant women were on insulin therapy [10]. In our study, age has no effect on the association between GDM and PCOS.

17% of PCOS pregnant women developed hypothyroidism. This shows that there is an increased risk (OR 5.869) of hypothyroidism in GDM women. In a study, "Relationship between hypothyroidism and the incidence of gestational diabetes": A meta-analysis showed results that overt hypothyroidism was associated with an increased risk of gestational diabetes with Odd's Ratio of 1.892, (95% CI 1.679-2.132, $p < 0.001$). The relative risk of gestational diabetes was also increased in subclinical hypothyroid [12].

PCOS per se is characterised by hyperandrogenism, menstrual irregularities, insulin resistance and obesity. Out of the 56 PCOS pregnant women 35% had irregular cycles, 16 % had hirsutism, 20% had acne, 21% had acanthosis, 85% have scan finding suggestive of PCOS [9, 16]. Studies like "Epidemiology, diagnosis, and management of polycystic ovary syndrome" have shown that PCOS had menstrual disturbances, infertility, early pregnancy loss and many pregnancy related complications like GDM as well [9].

Incidence of IUD, preterm birth, anomalous baby, big baby are almost same in both groups. There is no stronger association [6, 19].

33% of PCOS women have history of infertility, 16 % have conceived by ovulation induction & 16% on IVF/IUI conception [13, 14].

Both GDM and PCOS have strong genetic involvement and family history. 21% of PCOS women have H/O diabetes mellitus in family members. PCOS women who have the family history of diabetes developed GDM [20].

Previous history of GDM plays a significant role. 15 % of PCOS pregnant women have history of GDM in the past pregnancy in our study. Recurrence rates of up to 70% have been reported in index pregnancies according to a study named, "Recurrent gestational diabetes: risk factors, diagnosis, management, and implications" [11].

It is important to educate the mother and her family about the dietary recommendation, exercise, blood sugar monitoring, administration of insulin, for regular follow up during and after delivery and should have knowledge regarding the complication of GDM to herself and her baby.

Conclusion

Gestational Diabetes Mellitus and PCOS are emerging diseases and is also becoming a major health issue in this era. As women of reproductive age group have problems with their menstruation, fertility, become obese and succumb mental trauma in relation to this. In our study, we have concluded that women with previous history of PCOS have high risk of development of gestational diabetes mellitus. These conditions

also have genetic influences and hence pass over from one generation to the other, thus posing a threat. About half of GDM mothers develop type 2 DM later in their life which needs careful follow-up and lifestyle modifications. Babies born to Diabetic mother experience many complications in their early life. Now these two conditions together have become a public health issue and the Government of India has launched schemes to help health workers simplify the issue. Adequate education, improving socio-economic status are also the hurdles faced by the policy makers. People must adhere to the guidelines given so the GDM can be diagnosed and treated earlier. Awareness and proper counselling are needed for the adolescents. Thus, to conclude, both GDM and PCOS are public health issues that needs to be diagnosed and treated appropriately so that it doesn't affect the quality of life of these individuals.

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Conflict of Interest

Not available

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