ORIGINAL ARTICLE

FREQUENCY OF GESTATIONAL DIABETES MELLITUS AND THE ASSOCIATED RISK FACTORS AMONG WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Background: Polycystic Ovary Syndrome (PCOS) is a significant risk factor for developing Gestational Diabetes Mellitus (GDM). The objective of this study was to determine the frequency of GDM and the associated risk factors among women with PCOS. **Methods:** This cross-sectional study was done at CMH, Dera Ismail Khan from Aug 2023 to Aug 2024. Participants underwent 75 g Oral Glucose Tolerance Test (OGTT) between 24–28 weeks as part of screening for GDM. Data was analysed on SPSS-24. Shapiro-Wilk test, Mann-Whitney test, Independent *t*-test, and Chi-square test were applied, and $p \leq 0.05$ was considered statistically significant. **Results:** The study included a total of 296 pregnant women with 148 (50.0%) having PCOS and 148 (50.0%) without PCOS. The frequency of GDM was 45.3% and 27.7% among PCOS and non-PCOS women respectively. There existed a significant variation between the GDM and non-GDM groups with reference to the current menstrual status ($p<0.001$) and menstrual patterns ($p=0.007$). The use of metformin was significantly associated with reducing the occurrence of GDM ($p=0.002$). No statistically significant differences were observed in serum levels of LH ($p=0.797$), FSH, and free testosterone level between the GDM and non-GDM groups. **Conclusion:** Women with PCOS are at higher risk of developing GDM. GDM screening should be offered at 24–28 weeks in PCOS women with history of irregular menses.

Keywords: Gestational diabetes mellitus, GDM, Polycystic ovary syndrome, PCOS, glucose level, GTT

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INTRODUCTION

Pregnancy typically leads to higher insulin resistance caused by the secretion of hormones including growth hormone, oestrogen, lactogen, tumour necrosis factor-alpha, and progesterone.[1] Gestational diabetes mellitus (GDM) occurs when a hormone produced by the placenta interferes with the body's ability to use insulin properly. As a result, glucose accumulates in the blood rather than being absorbed by the cells. It is categorized based on the treatment needed: Type A1GDM refers to cases managed with diet changes; while Type A2GDM involves the use of medication.[2] Gestational diabetes mellitus is a common health issue in pregnancy that arises primarily during the second and third trimesters. It affects 5–10% of pregnancies in the US[3] and 4.41–57.90% of pregnancies in Pakistan. Screening includes review of patient's history, family history of type 2 diabetes, oral glucose tolerance test (OGTT), as well as the previous obstetrical history. A 75 g OGTT is used for screening of GDM at 24–28 weeks in individuals not previously diagnosed with diabetes. In OGTT plasma glucose level is measured when patient is fasting and at 1 and 2 hour after glucose ingestion.[4]

Two probable causes of GDM have been recognized: pancreatic β-cell dysfunction and impaired responsiveness to glycaemic levels.[5] Significant insulin resistance produced by hormonal secretions such as lactogen, prolactin, growth hormone, and progesterone results in a delayed response to glycaemic levels. GDM can be treated with lifestyle modification as well as with medications like metformin and insulin to attain optimum glycaemic control.[6]

Preeclampsia, an increased chance of caesarean birth, and a high probability for type-two diabetes mellitus are amongst the maternal complications of GDM. Foetal macrosomia, shoulder dystocia, foetal hyperglycaemia, neonatal hypoglycaemia, respiratory distress syndrome and elevated perinatal mortality are examples of foetal problems that may arise.[7] These complications can be reduced by obtaining an optimal glycaemic control during pregnancy.

The most prevalent endocrine pathology in women during their reproductive ages is polycystic ovary syndrome (PCOS), a multifactorial problem.[8] Due to the impacts of puberty, PCOS symptoms might be difficult to diagnose in the early stages of pubertal years. It was first identified in 1935, the prevalence currently varies from 5–15%.[9] Since numerous conditions can resemble the clinical characteristics of PCOS including Congenital Adrenal Hyperplasia, thyroid disease and hyperprolactinemia, the diagnosis is one of exclusion. The Rotterdam criteria define PCOS as having a minimum of two of the following

conditions: irregular menstrual cycles, polycystic ovaries (PCO), and hyperandrogenism. There are several other symptoms associated with PCOS, the most frequent ones being baldness, infertility, and hirsutism.[10,11] Women who have previous diagnosis of the GDM were more prone to have PCOS than non-PCOS women, and that PCOS individuals were at greater risk of developing GDM in future.[12]

The purpose of this study is to determine frequency of GDM and the associated risk factors among women with PCOS.

METHODOLOGY

This cross-sectional study was carried out in CMH, Dera Ismail Khan from August 2023 to August 2024, with approval from the Institutional Review Board under reference number A/14/ERC/07/23. After a comprehensive literature search, we used the WHO calculator to establish a sample size of 296 with a margin of error of 5%, a confidence level of 95%, and GDM prevalence of 26% in pregnant women with PCOS.[13]

All women with singleton pregnancy who received prenatal care at CMH, Dera Ismail Khan were included in this study. All patients provided written agreement prior to enrolment. Exclusion criteria were age ≥40 years, family history of diabetes, previously history of gestational diabetes, pre-existing diabetes, stillbirth, untreated hypothyroidism, delivery of babies weighing ≥4 Kg, history of recurrent miscarriages, congenital adrenal hyperplasia, Cushing's syndrome, and/or hyperprolactinemia.

The PCOS was confirmed when a minimum of two of the Rotterdam criteria were met, which include oligomenorrhea or amenorrhea, at least one hyperandrogenism symptom (such as acne, hirsutism, or significant hair loss), and polycystic ovaries found via ultrasound.[14] At 24 to 28 weeks of pregnancy, all participants underwent a 75 g OGTT.

Levothyroxine (LT4) was given to hypothyroid women both before and during the pregnancy to keep their TSH levels below 4.0 mIU/L before conception. Most women with PCOS were already taking metformin three months before pregnancy, depending on the severity of the condition and the woman's BMI.

Data was analysed using SPSS-24. For the categorical data, frequencies and percentages were determined. For the continuous data, Mean±SD were calculated. Shapiro-Wilk test was utilized for checking the distribution in data. The Independent *t*-test as well as the Mann-Whitney test was used for comparison of the variables between study groups for data that was not normally distributed and normally distributed, respectively. Chi-square test was used for comparison of the categorical variables, and $p \leq 0.05$ was considered statistically significant.

RESULTS

The study included 296 pregnant women, including 148 (50.0%) having PCOS and 148 (50.0%) without PCOS. The mean age of the participants was 28.87±4.62 years. Prevalence for GDM was 27.7% and 45.3% for non-PCOS pregnant women and PCOS women respectively ($p<0.001$) (Table-1).

There existed a significant variations between the two groups with reference to the current menstrual status ($p<0.001$) and menstrual patterns ($p=0.007$). The findings indicated that the use of metformin was significantly associated with reducing occurrence of GDM ($p=0.002$). Anyhow, no significant variations were observed in the pre-pregnancy BMI ($p=0.137$) or hirsutism ($p=0.397$) between the groups with and without GDM. (Table-2).

Table-3 compares the pre-pregnancy laboratory tests and hormonal profiling of women along with PCOS, distinguishing between those with and without GDM. The results did not reveal any statistically significant variation of luteinizing hormone (LH) level in serum sample ($p=0.797$), free testosterone ($p=0.382$), and follicle-stimulating hormone (FSH) ($p=0.333$) between the two groups.

Table-1: Prevalence of GDM in PCOS and Non-PCOS patients [n (%)]

Variables		PCOS (n=148)	Non-PCOS (n=148)	*p*
GDM Status	Yes	67 (45.3)	41 (27.7)	0.001
	No	81 (54.7)	107 (72.3)	

Table-2: Characteristics of women in non-GDM and GDM groups having PCOS [n (%)]

Variables		GDM (n=67)	Non-GDM (n=81)	*p*
Current Menstrual Status	Irregular	67 (100)	60 (74.1)	<0.001
	Regular	0	21 (25.9)	
Pre-Pregnancy BMI Level	<25	19 (28.4)	31 (38.3)	0.137
	≥25	48 (71.6)	50 (61.7)	
Menstrual Pattern	Normal	7 (10.4)	25 (30.9)	<0.01
	Oligo menorrhea	57 (85.1)	48 (59.3)	
	Amenorrhea	1 (1.5)	4 (4.9)	
	Poly menorrhea	2 (3.0)	4 (4.9)	
Pre Gestational Use of Metformin	Yes	30 (44.8)	56 (69.1)	<0.01
	No	37 (55.2)	25 (30.9)	
Hirsutism	<8	33 (49.3)	37 (45.7)	0.397
	>8	34 (50.7)	44 (54.3)	

Table-3: Pre-pregnancy laboratory tests of non-GDM and GDM groups in PCOS women (Mean±SD)

Hormones	GDM (n=67)	Non-GDM (n=81)	*p*
LH (mg/dL)	8.63±2.97	8.51±2.66	0.797
FSH (mg/dL)	6.85±1.52	6.62±1.36	0.333
Free Testosterone (ng/dL)	1.51±0.84	1.40±0.73	0.382

DISCUSSION

Polycystic ovary syndrome (PCOS) involves a variety of reproductive symptoms, including infertility and poor

metabolic conditions during and after pregnancy. PCOS women have been found to have intrinsic insulin resistance (IR), which can occur in up to 80% of cases.[15]

Most prior research has found a significant frequency of gestational diabetes in PCOS patients. Considering the wide variety of PCOS patients, including those who are obese with insulin resistance and others who are lean and insulin-sensitive, current study aimed for evaluation of the risk factors linked to the gestational diabetes among individuals with PCOS. The research specifically focused on identifying which types of PCOS are more prone to get gestational diabetes mellitus after accounting for established risk factors.

Our study results revealed that women having PCOS were having more chances of developing GDM. M. Ashrafi *et al*[16] also found higher prevalence of GDM in women with PCOS compared to the women with non-PCOS. Levran *et al*[17], Radon *et al*[18], as well as Reyes-Muñoz *et al*[19] also revealed that the occurrence of GDM was 19.2%, 40.9%, as well as 26.9% among PCOS women, contrasted with the 3%, 9.4%, as well as 9.6% respectively in women without PCOS. Turhan *et al*[20] concluded that there was no noticeable variation in the rate of GDM among PCOS and non-PCOS women.

Our study also found that out of 148 PCOS patients 71.6% of GDM patients and 61.7% of non-GDM patients were overweight. These results revealed that there is no significant association between BMI and GDM and non-GDM status. M. Ashrafi *et al*[16] also found that out of total PCOS patients 66.3% of the GDM patients and 60% of the non-GDM patients were overweight and there was no significant association among GDM and BMI in women with PCOS. Current study also revealed that there is reduction in the occurrence of GDM if the patient is using metformin prior to conception similar to M. Ashrafi *et al*[16] and Khattab *et al*[21].

Another finding of our study was that there was no significant association of serum LH, FSH and free Testosterone between the GDM and non-GDM patients. This means that level of hormones changes is not linked with the GDM status in PCOS patients. M. Ashrafi *et al*[16] also reported similar results.

The primary outcome of our study is to identify those risk factors which predispose women with PCOS more to occurrence of Gestational diabetes mellitus. Keeping in view these risk factors, screening of GDM should be offered to women at 24–28 weeks for early diagnosis and management which can reduce maternal and foetal complications such as macrosomia, preeclampsia, and caesarean delivery. This study also provides the healthcare guidelines and contributes to provide the guidelines for understanding the relationship of GDM with PCOS.

LIMITATIONS OF THE STUDY

The major limitation in our study was that it was performed in single centre and has limited size of sample.

CONCLUSION

Women with PCOS face an increased risk of developing GDM. Those with irregular menstrual cycles are particularly more susceptible and should undergo screening for GDM between 24–28 weeks of pregnancy.

RECOMMENDATIONS

For more accurate results we recommend that this study should be conducted on a larger scale.

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REFERENCES

1. Szlapinski SK, Hill DJ. Metabolic adaptations to pregnancy in healthy and gestational diabetic pregnancies: the pancreas-placenta axis. Current Vasc Pharmacol 2021;19(2):141–53.
2. Gică N, Huluță I. Gestational Diabetes Mellitus. In: Chlup R, (Ed). Type 2 Diabetes in 2024 —From Early Suspicion to Effective Management. IntechOpen; 2023.
3. Coustan DR. Diabetes in pregnancy. In: Winn HN, Chervenak FA, Romero R, (Eds). Clinical maternal-fetal medicine. CRC Press; 2021.p. 16.1–9.
4. Bhavadharini B, Mohan V. Gestational diabetes mellitus: Screening diagnosis, and management. In: Mohan V, Shekar MA, Rao GHR, (Eds). Current trends in diabetes focus on South Asians. JAYPEE Brothers; 2021.p. 247–57.
5. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. Int J Mol Sci 2018;19(11):3342.
6. Oskovi-Kaplan ZA, Ozgu-Erdinc AS. Management of gestational diabetes mellitus. In: Islam SM, (Ed). Diabetes: from Research to Clinical Practice. Cham: Springer; 2021.p. 257–72.
7. Moon JH, Jang HC. Gestational diabetes mellitus: diagnostic approaches and maternal-offspring complications. Diabetes Metab J 2022;46(1):3–14.
8. Joham AE, Norman RJ, Stener-Victorin E, Legro RS, Franks S, Moran LJ, *et al*. Polycystic ovary syndrome. Lancet Diabetes Endocrinol 2022;10(9):668–80.
9. Mishra S, Pal S, Tiwari M. Polycystic ovarian syndrome: A literature Review. Int J Yogic Hum Mov Sports Sci 2023;8:32–4.
10. Adone A, Fulmali DG. Polycystic ovarian syndrome in adolescents. Cureus 2023;15(1):e34183.
11. Siddiqui S, Mateen S, Ahmad R, Moin S. A brief insight into the etiology, genetics, and immunology of polycystic ovarian syndrome (PCOS). J Assist Reprod Genet 2022;39(11):2439–73.
12. Toulis KA, Goulis DG, Kolibianakis EM, Venetis CA, Tarlatzis BC, Papadimas I. Risk of gestational diabetes mellitus in women with polycystic ovary syndrome: a systematic review and a meta-analysis. Fertil Steril 2009;92(2):667–77.
13. Slouha E, Alvarez VC, Gates KM, Ankrah NM, Clunes LA, Kollias TF. Gestational diabetes mellitus in the setting of polycystic ovarian syndrome: A systematic review. Cureus 2023;15(12):e50725.
14. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care 2004;27(Suppl1):S88–90.

15. Bahri Khomami M, Joham AE, Boyle JA, Piltonen T, Silagy M, Arora C, *et al*. Increased maternal pregnancy complications in polycystic ovary syndrome appear to be independent of obesity –A systematic review, meta-analysis, and meta-regression. Obes Rev 2019;20(5):659–74.
16. Ashrafi M, Sheikhan F, Arabipoor A, Hosseini R, Nourbakhsh F, Zolfaghari Z. Gestational diabetes mellitus risk factors in women with polycystic ovary syndrome (PCOS). Eur J Obstet Gynecol Reprod Biol 2014;181:195–9.
17. Levran D, Shoham Z, Habib D, Greenwald M, Nebel L, Mashiach S. Glucose tolerance in pregnant women following treatment for sterility. Int J Fertil 1990;35(3):157–9.
18. Radon PA, McMahon MJ, Meyer WR. Impaired glucose tolerance in pregnant women with polycystic ovary syndrome. Obstet Gynecol 1999;94(2):194–7.
19. Reyes-Muñoz E, Castellanos-Barroso G, Ramírez-Eugenio BY, Ortega-González C, Parra A, Castillo-Mora A, *et al*. The risk of gestational diabetes mellitus among Mexican women with a history of infertility and polycystic ovary syndrome. Fertil Steril 2012;97(6):1467–71.
20. Turhan NÖ, Seckin NC, Aybar F, Inegöl I. Assessment of glucose tolerance and pregnancy outcome of polycystic ovary patients. Int J Obstet Gynecol 2003;81(2):163–8.
21. Khattab S, Mohsen IA, Aboul Foutouh I, Ashmawi HS, Mohsen MN, Van Wely M, *et al*. Can metformin reduce the incidence of gestational diabetes mellitus in pregnant women with polycystic ovary syndrome? Prospective cohort study. Gynecol Endocrinol 2011;27(10):789–93.

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