Impact of metformin on pregnancy outcomes in women with PCOS

Submitted by

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Abstract

Aim of study: To determine the effect of metformin on the outcome of pregnancy among women with PCOS in Al-Batool teaching hospital

Patients and methods: This is a cross sectional study. It was conducted in the period from July 2023 to January 2024. We collected 100 patients who have been diagnosed with PCOS and taking metformin as therapeutic agent for insulin resistance. We collected the sample from the patients who attend Al-Batool teaching hospital. We collected informations about age, BMI, random blood sugar tests, renal indices test, pregnancy outcomes, etc.

Results: 100 patients were enrolled in our study. 49% of them had family history of PCOS and 51% didn't. 13% of them were chronic cases of DM and 87% were healthy. 90% of them had live babies, there was no significant difference between use of metformin and pregnancy outcomes.

Conclusion: The use of metformin in pregnancy seems to be safe and protective against congenital anomalies in women with PCOS.

Introduction

The most prevalent endocrine disorder affecting women who are fertile globally is called polycystic ovarian syndrome, or PCOS. In 1935, Stein and Leventhal gave their first description. The prevalence can vary from 5% to 15% according on the diagnostic standards used. According to specialized society recommendations, PCOS must be diagnosed based on the presence of two out of the three criteria listed below: polycystic ovaries, clinical or biological hyperandrogenism, and chronic anovulation. Since it's an exclusion diagnosis, conditions that resemble PCOS's clinical characteristics must be ruled out. These include non-classical congenital adrenal hyperplasia, hyperprolactinemia, and thyroid illness. If clinical characteristics point to additional causes, a more thorough workup may be necessary for a specific patient (1).

PCOS is linked to a number of morbidities, such as endometrial cancer, depression, obstructive sleep apnea (OSA), obesity, metabolic syndrome, impaired glucose tolerance, type 2 diabetes mellitus (DM-2), endometrial cancer, and nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH). For each of these diseases, there are several screening guidelines; nonetheless, if a patient exhibits any sign of PCOS, the clinician needs to be willing to proceed with a workup regardless of the threshold (2).

PCOS is a complicated illness. Numerous susceptibility genes have been found to play a role in the disease's pathogenesis. These genes participate in androgenic pathways and steroidogenesis at different levels. About 70% heritability has been estimated from twin studies. The expression of these genes, as well as the onset and course of the illness, are significantly influenced by the environment. According to two widely accepted theories, PCOS traits manifest in people who have a genetic predisposition and are exposed to specific environmental variables. Two of

the most prevalent environmental factors are insulin resistance and obesity. Fetal androgen exposure is another theory that has been put out (3).

Primary abnormalities in the hypothalamic-pituitary axis, insulin secretion and action, and ovarian function are involved in the pathogenesis of PCOS. Despite having no recognized etiology, obesity and insulin resistance have been connected to PCOS. It makes sense that there would be a connection between insulin and ovarian function—excess insulin causes the ovaries to produce androgens, which can cause anovulation. The primary indicator of an ovarian anomaly is follicular maturation arrest (4).

PCOS is a hormonal condition that can cause a number of other illnesses. It also remains a common cause of female infertility. The three most prevalent characteristics linked to PCOS are irregular ovulation, elevated testosterone levels, and cystic ovaries, though signs and symptoms can vary. For most women with PCOS, ovulation issues and increased testosterone levels are the norm. Moreover, polycystic ovaries are more common on pelvic ultrasonography than 70% in PCOS patients, and hirsutism, acne, and alopecia are all strongly linked to increased androgen levels (5).

Treatment for PCOS focuses on symptom management because the underlying cause is unknown. While there are treatment options for the syndrome, not all of them are completely effective, and the patient's desire to become pregnant may keep her from seeking help even when her symptoms are present. Reducing insulin resistance, stopping the action of androgens on target tissues, and treating anovulation should all be treatment objectives (6).

Anti-diabetic medications can lower insulin resistance, lower circulating testosterone levels, and increase fertility. When it comes to treating PCOS,

metformin has more data available than thiazolidinediones. In a trial including 320 women, the effectiveness of metformin versus placebo for treating infertility associated with PCOS was examined. Both groups were permitted to add an adequate infertility medication to their regimen after three months of treatment without any resultant pregnancy. When compared to a placebo, metformin was linked to noticeably greater rates of pregnancy (7).

Aim of study

To determine the effect of metformin on the outcome of pregnancy among women with PCOS in Al-Batool teaching hospital.

Patients and methods

This is a cross sectional study. It was conducted in the period from July 2023 to January 2024. We collected 100 patients who have been diagnosed with PCOS and taking metformin as therapeutic agent for insulin resistance . We collected the sample from the patients who attend Al-Batool teaching hospital. We collected informations about age, BMI, random blood sugar tests, renal indices test, pregnancy outcomes, etc. we collected the information using prepared written questionnaire and by direct interview with the patients. We preserved the privacy and we coded the patients for the reasons of confidentiality and risk of bias.

Statistical analysis

SPSS Version 25 was used for the description of the data. We expressed the quantitative data by arithmetic mean, standard deviation and mode and the qualitative data by frequencies. Chi square and t-test was used to identify the association between the variables when P value less than 0.05 considered significant.

Results

100 patients were enrolled in our study. Their general gynecological information is demonstrated in table 1.

Table 1. gynecological information

		Mean	Count
Age		30.81	
para	1.00		28
	2.00		23
	3.00		32
	4.00		7
	5.00		8
	6.00		2
Gravida	1.00		5
	2.00		33
	3.00		25
	4.00		24
	5.00		2
	6.00		7
	10.00		2
	12.00		2
Abortion	.00		40
	1.00		39
	2.00		15
	3.00		2
	6.00		4

The socioeconomic state is demonstrated in table 2.

Table 2. socioeconomic state

State	Frequency	Percent
Low	23	23.0
Moderate	69	69.0
High	8	8.0
Total	100	100.0

Table 3 demonstrate the BMI values in our study.

Table 3. BMI values.

BMI	Frequency	Percent
18.5-24.5	37	37.0
24.5-28.5	57	57.0
> 28.5	6	6.0
Total	100	100.0

49% of them had family history of PCOS and 51% didn't. 13% of them were chronic cases of DM and 87% were healthy. The values of their RBS, RFT before and after labour is demonstrated in table 4.

Table 4. The values of their RBS, RFT before and after labour

Values	Mean
RBS before pregnancy	109.15
RBS after pregnancy	105.84
Urea before pregnancy	22.90
Urea after pregnancy	22.90
Creatinine before pregnancy	1.73
Creatinine after pregnancy	.66

Table 5 demonstrate the pregnancy outcomes

Table 5. pregnancy outcomes

		Count	%
Use of metformin	Until pregnancy	75	75
	After pregnancy	25	25
Pregnancy outcome	Live	90	90
	Stillbirth	2	2
	Aborted	8	8
Maturity	Term	80	80
	Preterm	20	20
Congenital anomalies	Yes	6	6
	No	93	93

The association between metformin and pregnancy outcome is demonstrated in table 6.

Table 6. association between metformin usage and pregnancy outcomes

Metformin use		Pregnancy outcome				Sig.
		Live	Stillbirth	Aborted	**Total**	
Use of metformin	Until pregnancy	68	2	5	75	0.510
	After pregnancy	22	0	3	25	
Total		90	2	8	100	

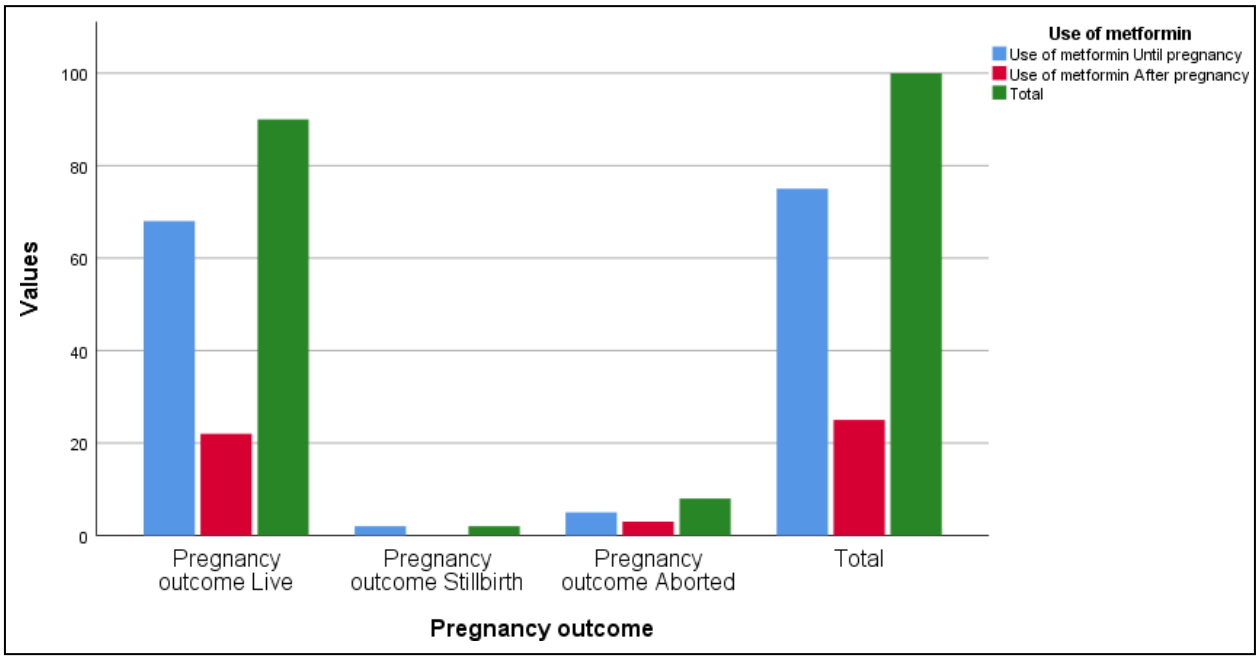

Figure 1. Table 6. association between metformin usage and pregnancy outcomes

Discussion

We observed improved pregnancy outcomes in our investigation, even though we started with a higher baseline risk due to greater glucose intolerance. Babies that received metformin therapy had fewer congenital abnormalities. Although not statistically significant ($P > 0.05$), these findings support the use of metformin in PCOS patients.

There is growing evidence that increased insulin resistance is linked to the fundamental pathophysiology of PCOS. Metformin is one example of an insulin sensitizer that may help treat PCOS. There are ambiguities about the appropriate dose and timing of metformin withdrawal. Concerning potential danger to the fetus, several experts advised stopping metformin once the pregnancy was verified. Nonetheless, there is proof that metformin does not cause birth defects (8).

Ehrmann believed that PCOS was linked to worse pregnancy outcomes and that treating pregnant women with PCOS with metformin may lessen pregnancy complications (9). Ben-Haroush et al. contended that women with PCOS had a higher miscarriage rate than the general female population. As a result, they recommend persistent use of metformin during the first trimester in the hopes of reducing the incidence of EPL. According to a retrospective research, women with PCOS who took metformin during their pregnancy had a lower chance of miscarrying in the first trimester (10).

While there is a growing body of research supporting the safety of taking metformin continuously during pregnancy, there has never been any mention of an elevated risk of congenital defects. After investigating the impact of metformin on expectant mothers, Coetzee and Jackson (11) came to the conclusion that there was no increased risk of significant congenital defects. The perinatal outcomes in

metformin-treated and control pregnancies were compared in a retrospective analysis (12), which revealed that the frequencies of congenital abnormalities, neonatal unit admission, and growth deficits were either similar in both groups or less common in the metformin-treated group.

Conclusion

The use of metformin in pregnancy seems to be safe and protective against congenital anomalies in women with PCOS. More studies should be conducted to insure and confirm our findings.

Recommendation

We recommend continuous use of metformin for pregnant women who have been diagnosed with PCOS as it has major effect on insulin resistance, blood sugar control and better pregnancy outcomes. We also recommend performing educational campaigns to demonstrate the benefits of metformin for all PCOS patients especially the pregnant women.