



ORIGINAL ARTICLE

Analysis of efficacy of metformin in pregnant women with Polycystic Ovarian Syndrome (PCOS).

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ABSTRACT... Objective: To analyze of efficacy of metformin in pregnant women with POCS regarding occurrence of gestational diabetes mellitus. To analyze parity distribution for efficacy of metformin regarding occurrence of gestational diabetes mellitus in pregnant women with POCS. **Study Design:** Descriptive Cases Series. **Setting:** Sheikh Zaid Hospital, Lahore. **Period:** July 1, 2019 to December 31, 2019. **Methods:** Till delivery 200 pregnant ladies were followed up to see if they developed GDM or not. A pre-prepared form was used to record metformin efficacy frequency and GDM in pregnant ladies with PCOS. For efficacy and parity (qualitative variables), percentages and frequencies were got calculated using SPSS.16. **Results:** Thirty two (16%) women got '0' parity. Forty four (22%) got '1' parity. Fifty (25%) got '2' parity. Forty two (21%) got '3' parity. While thirty two women (16%) got '4' parity. Twenty two (78.57%) was efficacy for nulliparous patients. Thirty three (76.74%) was efficacy for primiparous patients. One hundred nine (84.50%) was efficacy for multiparous patients. Insignificant difference was noted as p was more than 0.05. In one hundred sixty six (83%) women metformin efficacy got achieved. **Conclusion:** Multiparous patients with PCOS showed relatively more efficacy (84.50%) of metformin against gestational diabetes mellitus while twenty five percent pregnant women with PCOS with a thorough use of metformin delivered two live neonates.

Key words: Distribution, Efficacy, GDM, Metformin, Parity, Poly Cystic Ovarian Syndrome, Pregnant Women.

INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is a medical entity comprising of enhanced androgenic levels, any cyst of ovary and menstrual irregularities.¹ Pakistani women had prevalence of PCOS in 20.7%.²

44.4 % cases had Gestational Diabetes Mellitus (GDM) in a research study which also documented that GDM is very often associated in pregnant with infertility and PCOS history.³ Other study on patients taking metformin showed that 90 % did not encounter GDM and mere 10 % were affected with it despite they took metformin. Some similar research study documented that 44 % patients who took metformin suffered GDM and 96.65% not had that.⁴ Morphological form manifested with PCOS while biochemical form manifested with hyperandrogenemia. If hyperandrogenism, there was inhibition of follicle development,

changes in menstrual cycle, ovary microcysts and none ovulation.⁵ Hyperinsulinaemia, resistance against insulin with affected glucose tolerance was manifested in women who had body mass index lesser than 30 (despite insulin resistance might be there in thin women affected with PCOS).⁶ Metformin augments insulin sensitivity and hence improved plasma glucose control. Patients having PCOS encountered hypertension, GDM and early stage pregnancy loss more than those in who did not have PCOS and benefits were documented if metformin was taken throughout pregnancy.⁷

We adopted this research because literature was found to be limited in finding parity distribution for metformin efficacy against GDM in pregnant women having polycystic ovarian disease.

METHODS

At Sheikh Zaid Hospital Lahore a study (descriptive

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case series) was carried out from July 1, 2019 to December 31, 2019 after being ethically approved (CPSP/REU/OBG-2014-072-6464) (04.10.17). None probability consecutive sample technique used. Till delivery 200 pregnant ladies were followed up to see if they developed GDM or not (% age of efficacy expected considered as 90 % and with error margin 4 % the confidence level was 95 %). PCOS diagnosed pregnant women and metformin prescribed and taken unstopped in thorough pregnancy, 25-40 years age, and any type of parity and after 28-30 pregnancy weeks were included. As per record or history formerly diagnosed cases of diabetes mellitus, hypertension, hypothyroidism, women who had more than 3 miscarriages were excluded. After consent being taken from participant patients, a pre-prepared form was used to record metformin efficacy frequency and GDM in pregnant ladies with PCOS. General Physical Examination for PCOS after history was carried out. They were followed up till their delivery process to document presence/absence for GDM.

Operational Definitions

The efficacy of metformin was considered if the patients did not develop Gestational Diabetes Mellitus at 28, 32, 36 weeks of gestational and 6 weeks postpartum while parity was considered as the number of times a woman has given birth to live neonate (any gestation) or at 24 weeks or more regardless of whether the child was viable or non-viable (i.e still births).

Data obtained after biases control was stratified for frequency of metformin efficacy and parity distribution. SPSS.16 was used to analyze data so collected. For efficacy and parity (qualitative variables), percentages and frequencies were got calculated. Effect modifiers were dealt accordingly. To see significance Chi-square was got applied. Significant p-value was less or equal to 0.05.

RESULTS

Thirty two (16%) women got ‘0’ parity. Forty four (22%) got ‘1’parity. Fifty (25%) got ‘2’ parity. Forty two (21%) got ‘3’parity.While thirty two women (16%) got ‘4’ parity (Figure-1).

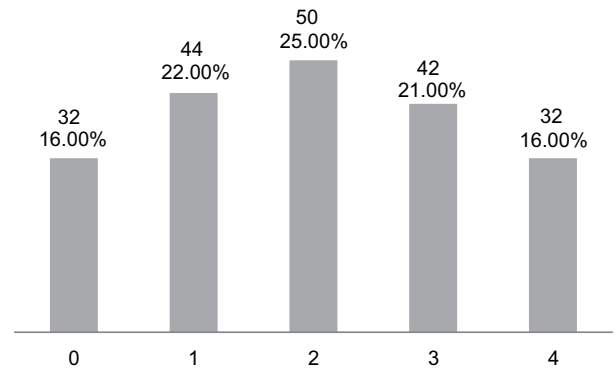


Figure-1. Parity distribution of females

Regarding patient’s parity, stratification of data was done. Twenty two (78.57%) was efficacy for nulliparous patients. Thirty three (76.74%) was efficacy for primiparous patients. One hundred nine (84.50%) was efficacy for multiparous patients. Insignificant difference was noted as p was more than 0.05 (Table-I).

		Parity			Total
		Nulliparous (primigravida)	Primiparous	Multiparous	
Efficacy	Yes	22 78.57%	33 76.74%	109 84.50%	164 82.00%
	No	6 21.43%	10 23.26%	20 15.50%	36 18.00%
Total		28 100%	43 100%	129 100%	200 100%

**Table-I. Efficacy comparison regarding parity
Chi-Square Test (X² = 0.456)
p- Value = 0.79 (Insignificant)**

DISCUSSION

GDM was usually found in pregnant women having PCOS.⁸ In liver cells, Gluconeogenesis is suppressed and insulin sensitization is attained if metformin is used, hence its broader role against diabetes.⁹ Jamilian et al; discovered that twelve week isoflavone intake showed significant betterment at triglyceride, biomarkers of stress, markers of insulin resistance and hormonal levels.¹⁰ If metformin was used throughout pregnancy span, it was proved to be associated in reducing GDM in PCOS patients.¹¹ Metformin is of great value to prevent GDM.¹² Because of its role in glucose intolerance and infertility, it was being utilized along with other prescriptions minimizing

chances of abortion and pregnancy loss of first trimester. Not only that as it was beneficial for both fetus and the mother, it was prescribed in other pregnancy stages.¹³ In our study one hundred nine (84.50%) was metformin efficacy for multiparous patients. Suppressing androgenic levels with weight loss in polycystic ovarian syndrome patients, reasonable insulin sensitivity increase was documented with metformin.¹⁴ In current study 25% pregnant women with PCOS with a thorough use of metformin had parity to be 2. Additionally, preeclampsia risk was also reasonably reduced with its use. Improvement of lipoproteins (high density), blood pressure control (diastolic) and Body Mass Index was also documented in patients of polycystic ovarian syndrome after a trial use of metformin for a span of 36 months.¹⁵ Measurement of BMI showed that metformin has reasonable impact on pediatric growth. Studies also proved that it has significant role in decreasing the chances of macrosomia but simultaneously involved in increasing circumference of fetal head.¹⁶ Glibenclamide is less preferred substitute of insulin in comparison to metformin.¹⁷

Different global settings like Canada, UK and New Zealand endorse metformin use in GDM.¹⁸ Endocrine disorder PCOS affects reproductive age females and is considered as an untoward maternal and perinatal risk. The research explored; its association with and without metformin in maternal and neonatal outcome and chances of obesity in neonates born to such mothers.¹⁹ Even then the data was not sufficient to recommend metformin in all patients with polycystic ovarian syndrome. Any way the evidence regarding its efficacy for pregnancy and fertility outcomes is not unequivocal and thereby demanding further research on women of different ethnic backgrounds and having different ranges of B.M.I.²⁰

LIMITATIONS

Because the sample was collected from a single public hospital of a big city, this being the limitation.

CONCLUSION

Multiparous patients with PCOS showed relatively more efficacy (84.50%) of metformin against gestational diabetes mellitus while twenty five percent pregnant women with PCOS with a thorough use of metformin delivered two live neonates.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.


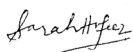
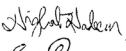
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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Sohail Anjum	1. Substantial contributed to conception or desing of the work or interpretation of data for the work.	
2	Sarah Hafeez Malik	2. Drafting of the work or revising it critically for important intellectual content.	
3	Nighat Nadeem	3. Final approval fo the version to be publisehd.	
4	Sohail Bashir Sulehria	4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.	