



## Co-morbid Gestational Diabetes and PCOS: Risks and Management

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### ABSTRACT

Diabetes is emerging global burden and is defined as chronic metabolic disorder that results in elevated level of blood glucose and is due to beta cell destruction. Gestational diabetes is the type of diabetes that occurs in women during pregnancy or first recognized at the Gestational period. The prevalence of Gestational diabetes is increasing tremendously in developing countries. Approximately 2 to 14% of pregnancy is diagnosed with Gestational diabetes and 90% of all Gestational diabetes is reported from low- and middle-income countries. Of these North Africa has the highest prevalence followed by South Asia. The chance of developing type 2 diabetes is 7 times higher in women with previous history of Gestational diabetes and also it involves in increasing the risk of cardio metabolic disorders in later life. Gestational diabetes results from various complex interactions of environmental, genetic and maternal factors. Polycystic ovarian syndrome (PCOS), a major cause of infertility in women causes hormonal abnormalities and is also associated with insulin resistance. There exists a relationship between Gestational diabetes and PCOS stating that PCOS increase the risk of Gestational diabetes since insulin resistance is common factor in both. It is observed that the risk of Gestational diabetes is threefold higher in women with PCOS. Both PCOS as well as Gestational diabetes affects the quality of life of women due to many pathological changes. Life style modification is essential for management of PCOS and Gestational diabetes. Insulin therapy is recommended to treat hyperglycemic condition during pregnancy.

**Keywords:** Gestational diabetes, Insulin resistance, Management, Obesity, Poly Cystic Ovarian Syndrome.

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### INTRODUCTION

Gestational diabetes is the intolerance of blood glucose level during pregnancy that results in risk of c- section delivery, hyperbilirubinemia and neonatal hypoglycemia.<sup>1</sup> The prevalence of Gestational diabetes is increasing over time and is associated with increase in obesity.<sup>2</sup> Risk of developing Gestational diabetes is 11 times more potent among Indian women.<sup>3</sup> Poly cystic ovarian syndrome is the most common heterogeneous disorder characterized by presence of cyst(s) in ovaries<sup>4</sup> and presence of 12 or more follicles . It affects about 21% women of reproductive age.<sup>5</sup> PCOS is associated with insulin resistance that results in abnormalities in androgen production and other metabolisms.<sup>6</sup> Poly cystic ovarian syndrome tends to increase the risk of Gestational diabetes since insulin resistance is the common anomaly in both and also incorporated with preeclampsia and preterm birth.<sup>7</sup> About 40% of women with poly cystic ovarian syndrome develop insulin resistance affecting quality of life in Gestational period.<sup>8</sup> As Gestational diabetes is one of the risk factors

for developing T2DM, poly cystic ovarian syndrome plays a key role in due time beta cell destruction increasing the risk further.<sup>9</sup> Thus PCOS being an endocrinal disorder affects quality of life of women in tremendous ways some of which includes metabolic and psychosocial disturbances.<sup>10</sup>

### Risks and Consequences

Gestational diabetes increases the risk of cesarean section delivery and premature rupture of membrane in women.<sup>11</sup> Antenatal depression is one of the major consequences of Gestational diabetes that has negative impact on patient's quality of life.<sup>12</sup> Women with previous history of Gestational diabetes have higher risk of developing type 2 diabetes mellitus and cardio vascular disease in later life.<sup>13</sup> Children born to mother with Gestational diabetes are more likely to develop childhood obesity and other metabolic disorders. Type 2 Diabetes Mellitus and cardiovascular disease are predominant in later life of those children born to diabetic mother.<sup>14</sup> Depression and stress are more common in women with PCOS when compared to other women.

### Pathophysiology

Poly cystic ovarian syndrome has a strong link with obesity and insulin resistance. Since insulin regulates ovarian functions, its resistance results in abnormal functioning of ovaries. Pathophysiology of PCOS includes abnormal gonadotropin - releasing hormone regulation that leads to increased secretion of luteinizing hormone and decreased level of follicle stimulating hormone. Response of follicle is



lowered because of the reduced level of follicle stimulating hormone that progress to follicle arrest.<sup>15</sup> PCOS leads to higher activity of serine phosphorylation causing abnormal behavior of serine. This leads to hyperinsulinemia and hence insulin resistance which accelerates diabetes in later life.<sup>16</sup> Fig.1 represents the short path of PCOS resulting in diabetes mellitus.



**Figure 1:** Brief pathophysiology of PCOS

### Management of PCOS and gestational diabetes

#### Pharmacological management:

Clomiphene and Letrozole are helpful for treating infertility. Letrozole is said to have higher ovulation rates.<sup>17</sup> Clomiphene citrate has been widely used in induction of fertility in women with PCOS but resistance to clomiphene citrate is being increased hence Intermittent clomiphene citrate serves as an alternate to clomiphene citrate.<sup>18</sup> Letrozole, an aromatase inhibitor works by increasing Follicle stimulating hormone and reducing estrogen level.<sup>19</sup>

Metformin is the first-line medication for metabolic manifestations and best ovulation induction agent for non-obese PCOS individual.<sup>20</sup> Metformin, being an oral hypoglycemic drug aids in increasing insulin sensitivity by reducing the level of circulating insulin in PCOS individual.<sup>21</sup> Spirinolactone is used in combination with metformin for management of PCOS in India.<sup>22</sup> Table 1 explains the mechanism of drugs used in treatment of PCOS.

**Table 1:** Drugs in use for poly cystic ovarian syndrome<sup>23</sup>

Drugs	Mechanism
Clomiphene	Induce ovulation Increase output of pituitary gonadotropins
Letrozole	Reduce the level of estrogen
Metformin	Reducing the level of circulating insulin Increase insulin sensitivity

Insulin, metformin and glyburide are used in course of diabetes management in pregnancy.<sup>24</sup> Insulin administration is the first line management for Gestational diabetes while use of oral hypoglycemic agent Metformin falls under category B for use in pregnancy.<sup>25</sup> Table 2 describes the regimen for gestational diabetes on basis of blood glucose level.

**Table 2:** Stages of Gestational diabetes mellitus and recommended regimen<sup>26</sup>

Blood glucose level	Therapy
Fasting <95mg/dl	Non pharmacological management. Diet and exercise
Fasting 95-114mg/dl	Metformin
Fasting 115-125mg/dl	Combination of metformin and glyburide
Fasting >126mg/dl	Insulin

#### Non pharmacological management:

Obesity is the common co morbid condition for PCOS hence weight loss and calorie restricted diet in obese individual is recommended.<sup>27</sup> Weight loss improves insulin resistance.<sup>28</sup> Regular exercise increase intra myocellular triacylglycerol concentration which induce lipid uptake and utilization thus resulting in improved insulin sensitivity.<sup>29, 30</sup> Exercise also improves blood circulation to skeletal muscle enhancing the stability of mediators involved in insulin signaling transduction.<sup>31</sup> Aerobic exercise increase free fatty acid oxidation and circulate glucose helping in management of PCOS.<sup>32</sup> Rectification of vitamin D deficiency, regular intake of omega 3 assist in management of PCOS by increasing follicle stimulating hormone sensitivity.<sup>33, 34</sup> Curcumin, the active constituent of turmeric increases corpus leutum production by reducing thickness of follicular sheath and also reduces insulin sensitivity. It also acts as protective factor and eliminates inflammation of PCOS.<sup>35, 36</sup>

Nutritious, balanced carbohydrate, protein and fat diet assist in rectification of poly cystic ovarian syndrome. Calorie intake should be divided into small meals and healthy snacks with low sugar drinks.<sup>37</sup> Cinnamon, one of the common spices have antioxidant, anti-hyperlipidemic, anti-diabetic and hepatoprotective properties. It enhances insulin sensitizing effect and help in improving menstrual regularity in PCOS.<sup>38</sup> Calorie required for PCOS individual ranges between 1800 and 2000 kcal per day. Increasing fiber rich food consumption aid in reducing insulin resistance and hyperandrogenemia.<sup>39</sup> Fiber rich foods including broccoli, cauliflower, bell peppers, sweet potatoes and pumpkin are good to consume. Anti-inflammatory foods like tomatoes, spinach, strawberries, turmeric help in reducing inflammation arising due to PCOS. Avoidance of processed meat, refined sugar and increased intake of anti-oxidants, omega 3, herbs are helpful in achieving target.<sup>40</sup>

#### CONCLUSION

Poly cystic ovarian syndrome is the emerging etiology of infertility and insulin resistance in later life of women. Poly cystic ovarian syndrome is considered as global burden since it affects mental health in addition to endocrine manifestations. Insulin resistance acts as a bridge between poly cystic ovarian syndrome and Gestational diabetes.

Incidence of Gestational diabetes increases as the rate of PCOS rises. This is because insulin resistance plays a dominant role in occurrence of Gestational diabetes which is induced by presence of poly cystic ovarian syndrome worsening the quality of life of both mother and child. Weight control association with balanced diet and exercise are initial steps in ceasing the complication of PCOS. Proper management of PCOS at early stage helps in decreased incidence of development of Gestational diabetes and other co morbid conditions.

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