# Letter to the Editor: " Gestational weight gain, appetite regulating hormones, and metformin treatment in polycystic ovary syndrome: A longitudinal, placebo- controlled study ".

Alishah Zehra[1] and Hussain Shah[1]

[1]Dow University of Health Sciences

June 27, 2022

**Title Page**

**Title:** Letter to the Editor: " Gestational weight gain, appetite regulating hormones, and metformin treatment in polycystic ovary syndrome: A longitudinal, placebo- controlled study ".

**Article type** : Letter to the editor.

**Correspondence:**

Syeda Alishah Zehra Contact: +92 347 2745652 Email: aiyakami123@gmail.com Address: Gulistan-e-Jauhar, Karachi. Affiliation: Dow University of Health Sciences, Karachi, Pakistan Department: Medicine.

**Co-authors:**

Hussain Haider Shah. Contact: +923163290773 Email: hussainhydershah03@gmail.com Address: Gulshan e Iqbal, Block 3, Karachi Affiliation: Dow University of Health Sciences, Karachi, Pakistan Department: Medicine.

**Words count:**

**Conflict of Interest:** None

**Declaration:** None

**Acknowledgment:** None

To the editor,

We read with keen interest the article by Johanna Molin et al. "Gestational weight gain, appetite regulating hormones, and metformin treatment in polycystic ovary syndrome: A longitudinal, placebo- controlled study".[1] It highlights the effects of appetite regulating hormones such as leptin, ghrelin and allopregnanolone on gestational weight gain (GWG) in pregnant women with Polycystic Ovary Syndrome (PCOS) and influence of metformin on these hormones. We concur with the findings that Metformin reduces the risk for excessive GWG and improves physiological leptin resistance in pregnant women with PCOS. However, a few points seem to us worth mentioning based on our experience that could boost the overall the quality of overall article.

In the original article the authors mainly emphasized on the effects of Metformin on GWG and maternal appetite regulating hormones but did not mention the possible effects of Metformin on fetal hormones due to intrauterine metformin exposure, Sex Hormone Binding Globulin (SHBG), a β-globulin protein possessing

high affinity binding for 17 beta-hydroxy steroid hormones such as testosterone and estradiol and its synthesis in liver is inhibited by Insulin. SHBG was elevated in the umbilical vein in newborn babies exposed to metformin in utero this would indicate that newborns of PCOS mothers are less insulin resistant if exposed to metformin in utero.[2] Furthermore, leptin in addition to being a key regulator of endocrine system has pro-inflammatory properties and it up regulates the secretion of inflammatory cytokines like IL-6, IL-12 and TNF-α. Serum leptin is elevated in many chronic inflammatory and autoimmune conditions including inflammatory bowel disease (IBD), endometriosis, type 1 diabetes mellitus, nephritis, nonalcoholic steatohepatitis (NASH), chronic obstructive pulmonary disease (COPD) , Bechet's disease and Grave's disease and rheumatoid arthritis.[3] This suggests that pregnant women with chronic inflammatory diseases could generate false positive result of increased free leptin levels.

Moreover, there is substantial evidence that Orlistat is as efficacious as metformin in reducing weight and attains similar ovulation rates in obese PCOS patients. However, Obese PCOS patients treated with orlistat showed significant improvements in lipid profile including LDL, Triglycerides, and total cholesterol at the end of 3 months of pregnancy and have minimal side-effects and is better tolerated compared with metformin.[4]

In conclusion, the exclusion criteria should include chronic inflammatory and auto immune diseases to exclude false positive results, known alcohol abuse as simultaneous consumption of alcohol and metformin could result in lactic acidosis, treatment with oral glucocorticoids or use of drugs known to interfere with pharmacokinetics of metformin. Moreover, the study population should also evaluate black and white ethnicities separately as Hispanic women with PCOS demonstrate severe phenotype in terms of hyperandrogenism and metabolism than non-Hispanic women. The author should also consider other drug regimens such as orlistat which is as efficacious as metformin with better benefits and lesser side effects.

REFERENCES:

1. Molin, J., Vanky, E., Løvvik, T. S., Dehlin, E., & Bixo, M. (2022). Gestational weight gain, appetite regulating hormones, and metformin treatment in polycystic ovary syndrome: A longitudinal, placebo-controlled study. *BJOG : an international journal of obstetrics and gynaecology* , *129* (7), 1112–1121. https://doi.org/10.1111/1471-0528.17042
2. Carlsen, S. M., & Vanky, E. (2010). Metformin influence on hormone levels at birth, in PCOS mothers and their newborns. *Human reproduction (Oxford, England)* , *25* (3), 786–790. https://doi.org/10.1093/humrep/dep444
3. Iikuni, N., Lam, Q. L., Lu, L., Matarese, G., & La Cava, A. (2008). Leptin and Inflammation. *Current immunology reviews* , *4* (2), 70–79. https://doi.org/10.2174/157339508784325046
4. Kumar, P., & Arora, S. (2014). Orlistat in polycystic ovarian syndrome reduces weight with improvement in lipid profile and pregnancy rates. *Journal of human reproductive sciences* , *7* (4), 255–261. https://doi.org/10.4103/0974-1208.147492