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**Short Communication** 

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## **Bariatric Surgery in Obese Women with Polycystic Ovarian Syndrome**

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"Because we focused on the snake, we missed the scorpion." – Egyptian Proverb

Obesity is one of the most common chronic conditions in the United States and globally. Worldwide, over 600 million adults can be classified as obese, and according to the National Health and Nutrition Examination Survey, nearly 38% of US adults have been classified as obese, and 8% as class III obesity (BMI  $\geq$ 40 kg/m<sup>2</sup>)<sup>1</sup>.

As it is well known, obesity increases the risk of adverse health outcomes including hypertension, dyslipidemia, coronary heart disease, stroke, type 2 diabetes, gallbladder disease, sleep apnea, osteoarthritis, cancer, mental illness, and all-cause mortality<sup>2-4</sup>. Compared to women with a healthy BMI (BMI 18.5-24.9 kg/m<sup>2</sup>), women with obesity are at increased risk of estrogen-mediated cancers, polycystic ovarian syndrome (PCOS), anovulation, and impaired fertility. With respect to the field of reproductive endocrinology and infertility, obese women face lower live birth rates following natural and assisted reproduction conception due to a combination of decreased pregnancy and implantation rates, as well as increased rates of miscarriage and pregnancy complications.

Interestingly, recent data reveal that 26% of women are overweight and 25% are obese prior to becoming pregnant, despite the recommendations of Institute of Medicine that preconception counseling should encourage women to aim to enter pregnancy with a healthy BMI<sup>5,6</sup>. This comes in light of studies suggesting that even modest reductions of up to 5% of pre-pregnancy weight appear to restore ovulation and improve fertility and birth outcomes<sup>7,8</sup>. First-line therapy for weight loss continues to be behavioral modification including reduced calorie diet and anorectic drugs; however, these interventions have largely been unsuccessful. Even those that do achieve weight loss have great difficulty in maintaining their weight<sup>2,9</sup>. Increased physical activity, even without weight loss, has also been shown to significantly improve pregnancy outcomes in obese women compared to those who do not engage in exercise<sup>10</sup>. It is thought that exercise, irrespective of weight loss, may improve insulin sensitivity, reduce inflammation and oxidative stress, thus improving reproductive function<sup>10,11</sup>.

A condition commonly associated with obesity is PCOS, which is the most common reproductive endocrinopathy affecting women of reproductive age; often associated with hirsutism, abnormal menstrual cycles, and glucose intolerance. While PCOS may be present in both obese and non-obese women, it is estimated that 50% - 65% of women with PCOS are overweight or obese<sup>12,13</sup>. Metabolic syndrome and obesity coexist commonly with PCOS women with associated glucose abnormalities, diabetes mellitus, dyslipidemia and consequently cardiovascular disease. Nonsurgical weight loss intervention has also been used as first-line management for PCOS<sup>14</sup>. Similar to non-PCOS obese women, loss of as little as 5% of initial body weight has been reported to dramatically improve hormonal abnormalities, menstrual cycle regularity, and fertility success rates<sup>8,14-19</sup>. However, a metaanalysis regarding lifestyle intervention concluded that although a healthy lifestyle decreased insulin resistance and hyperandrogenism, data is still lacking on its effects regarding pregnancy, live birth, and miscarriage<sup>20</sup>.

Bariatric surgery, which includes a variety of procedures, has also been recommended for women with a BMI  $\geq$ 40 kg/m<sup>2</sup> or with BMI  $\geq$ 35 kg/m<sup>2</sup> and comorbidities who have not benefited from non-surgical weight loss attempts<sup>21</sup>. Interestingly, historical references report the first bariatric surgery was performed on the King of Leon in the 10<sup>th</sup> century. The King of Leon was reported to be such an obese man that he could not walk, ride a horse, or pick up a sword which led him to lose his throne. He was treated by a famous doctor named Hasdai Ibn Shaprut, who sutured the kings' lips and consequently could only be fed on a liquid diet through a straw. He lost half his weight, and on his horse, he returned to Leon and regained his throne $^{22,23}$ . Surgical weight loss interventions remained in relative obscurity until 1954 when Kremen performed the first metabolic surgery referred to as the jejuno-ileal bypass surgery<sup>24</sup>. Since that time, surgical interventions have gained increasing momentum, from the first proposed "bariatric surgery" (or gastric bypass) in 1966 by Mason, when he noted that patients with subtotal gastrectomy for cancer lost a considerable amount of weight<sup>25</sup>, to the first laparoscopic gastric bypass by Wittgrove in 1994<sup>26</sup>. There has been an exponential growth of bariatric surgery, with an estimated 686,000 procedures performed worldwide in 2016 alone<sup>27</sup>.

*"Because we focus on the snake"*, long-term studies have shown that bariatric surgery result in significant longstanding loss of weight, recovery from diabetes, improvement in cardiovascular risk factors, and a reduction in mortality from 40% to 23%<sup>28</sup>. However, we shall not *"miss the scorpion."* According to a systematic review of weight loss interventions, data suggest bariatric surgery is more effective for weight loss than comprehensive behavior change and results in increased pregnancy and/or live birth rates after ART<sup>29</sup>. In one study all women who proceeded to undergo ART following bariatric surgery were able to conceive<sup>30</sup>. However, much remains to be clarified. Bariatric surgery does not come without risks or complications arising in subsequent pregnancies including internal hernias, bowel obstructions, hyperemesis, cholelithiasis, and gastric band-related complications<sup>3,4</sup>. The recommended time to avoid pregnancy is also still unclear, with current recommendations suggesting pregnancy be avoided for 6-12 months after 8

bariatric surgery due to metabolic and nutritional aberrations resulting from the procedure<sup>8</sup>. Even one-year post-surgery, long-term malabsorption and metabolic derangements may persist and impair reproductive outcomes<sup>31</sup>. Other risks reported include increased risk of small-for-gestational-age infant (OR=2.2, 95% CI: 1.64-2.95), increased risk of preterm birth between 32 weeks and 36 weeks and 6 days (OR=1.3, 95% CI: 1.05-1.6), and a trend for increased risks of stillbirth/neonatal death (OR=2.39, 95% CI: 0.98-5.85, p=0.06)<sup>32</sup>. Thus, it is important that women undergoing bariatric surgery receive long-term follow-up regarding nutrition, physical activity, and psychosocial health in order to ensure that the benefits of surgery are fully realized while minimizing adverse side effects. For each individual patient, the risks of surgical and medical weight loss therapies must be carefully considered and weighed against the benefits, given the expense and potential morbidity. Randomized clinical trials are still needed to clarify these issues of bariatric surgery.

While weight loss may have some benefits in improving fertility in women with increased BMI, it is a time-intensive. It is possible that the benefits of weight loss on fertility can be overshadowed by the negative impacts of advancing age. Some argue that age is more important than obesity in predicting successful ART, thus women with obesity should be counseled with this in mind, working closely with a multidisciplinary team to formulate individualized treatment plans based on each patient's unique circumstances<sup>33</sup>.

In conclusion, bariatric surgery is a powerful tool. At a minimum, every woman with PCOS wishing to conceive deserves to be offered education and counseling regarding the role of bariatric surgery in improving reproductive outcomes. Just as important, reproductive age women desiring pregnancy who undergo bariatric surgery should be included in research outcomes to improve our knowledge of long-term outcomes. Although there is convincing evidence suggesting favorable reproductive outcomes postoperatively, bariatric surgery should still be considered with caution, along with other medical and lifestyle alterations, as therapy in PCOS and non-PCOS women with obesity. Thus, "just because we focused on the snake, we must not miss the scorpion."

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