Normal pregnancy outcome after first-trimester exposure to semaglutide in an overweight woman: a case report

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Author contributions
Zhu XM collected patient’s information and wrote the manuscript. Huang QY, Chen Y investigated and searched literature. Zhou Y revised and finalized the manuscript. Yang CH was responsible for conceptualization, resources, supervision.

Competing interests
The authors declare no conflicts of interest.

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Abbreviations
GLP-1RA, glucagon-like peptide-1 receptor agonist; GW, gestational week; PCOS, polycystic ovary syndrome; HAIR-AN, hyperandrogenism-insulin resistance-acanthosis nigricans; T2DM, Type 2 Diabetes Mellitus.

Citation

Abstract
We reported a case of an overweight 34-year-old woman who unexpectedly became pregnant while undergoing semaglutide in early pregnancy and delivered a healthy male infant by caesarean section at 37 weeks and 4 days of gestation. Until now, the safety of semaglutide for use during pregnancy was unknown. This report may contribute to the limited knowledge available on pregnant women exposure to semaglutide.

Keywords: case report; glucagon-like peptide-1 receptor agonist; semaglutide; normal pregnancy outcome
**Background**

Semaglutide, a once-weekly, extremely long-acting glucagon-like peptide-1 receptor agonist (GLP-1RA) with a half-life of one week, has demonstrated significant hypoglycemic, weight-reducing and lipid-lowering effects, making it a preferred treatment option among patients [1]. As a result, utilization among fertile women and even those planning to become pregnant may increase in the future. However, animal studies have demonstrated that GLP-1RA may induce early pregnancy loss, fetal visceral abnormalities, and skeletal deformities [2, 3]. It is still uncertain whether these complications would manifest in pregnant women. To date, the safety of semaglutide for use during pregnancy is unknown, and only one case of normal pregnancy outcomes after first-trimester exposure to semaglutide has been reported in a woman with polycystic ovary syndrome (PCOS) [4]. Here, we present a case study of first-trimester exposure to semaglutide in an overweight woman, with the aim of enhancing our understanding of the limited knowledge available regarding the pregnancy outcomes after exposure to semaglutide in pregnant women.

**Case presentation**

A 34-year-old Chinese woman was diagnosed as overweight on May 17, 2022, and initiated treatment with semaglutide injection with 1 mg/week. Approximately 8 weeks later, she went to the hospital for 37 days of delayed menstruation and 3 days of vaginal bleeding. A serum β human chorionic gonadotropin level of 11,727.0 mIU/mL confirmed that she was pregnant with her second child at gestational week (GW) 5 + 2 and semaglutide was discontinued immediately. The final semaglutide injection was administered at GW 4 + 6. She experienced a weight loss of 2 kg and maintained a body mass index of 23 at the time of conception during her treatment. The woman, concerned about the toxic effects of semaglutide, visited a pharmacist's clinic at GW 6, where fetal ultrasound monitoring revealed an early intrauterine pregnancy with evidence of survival and an embryo bud measuring approximately 10 mm. The woman chose to continue with the pregnancy based on the recommendations of her clinical pharmacist and her personal inclination. She had no history of medication other than semaglutide injection in the first trimester. Her first child was delivered by cesarean section at GW 36 in 2014 due to intrauterine distress.

She had regular check-ups throughout her pregnancy, and all the results of the nuchal translucency test, thalassemia screening, oral glucose tolerance test, fetal gross malformation screening, and thyroid function were within normal limits. At GW 19, 22, 29, 30, 35, 37, ultrasound examination showed no abnormality in fetal growth and development, the parameters of the fetal growth chart were within the normal limits (Figure 1, Table 1).

Due to the “scar uterus and threatened labor”, the patient underwent a cesarean section at GW 37 + 4 on February 27, 2023. The newborn was a male with a weight of 3,120 g, a length of 49 cm. The postnatal pediatric examination revealed mild bipedal varus, micropenis but he was otherwise healthy.

**Discussion**

Currently, the primary indications for semaglutide are diabetes treatment and weight loss promotion. And also has been used for other indications, such as the treatment of subfertility related to diabetes, polycystic ovary syndrome [2, 3]. The pregnant woman in our report was treated up until GW 4 + 6. Because of the long half-life of semaglutide (approximately 1 week), the pregnant women in our case

![Figure 1](https://www.tmrjournals.com/tcr)

**Figure 1** Fetal weight estimation – National Institute of Child Health and Human Development. Definition: a birth weight below the 10th percentile for gestational age is defined as small for gestational age.

**Table 1** Fetal growth data at different GWs

<table>
<thead>
<tr>
<th>Gestational age (week)</th>
<th>Biparietal diameter (mm)</th>
<th>Head circumference (mm)</th>
<th>Abdominal circumference (mm)</th>
<th>Femur length (mm)</th>
<th>Estimated fetal weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 + 4</td>
<td>45</td>
<td>168.2</td>
<td>153.1</td>
<td>30</td>
<td>317</td>
</tr>
<tr>
<td>22 + 4</td>
<td>55</td>
<td>204.5</td>
<td>187.9</td>
<td>37</td>
<td>532</td>
</tr>
<tr>
<td>29 + 5</td>
<td>76</td>
<td>277</td>
<td>269</td>
<td>58</td>
<td>1,161</td>
</tr>
<tr>
<td>30 + 0</td>
<td>77</td>
<td>287</td>
<td>275.5</td>
<td>52</td>
<td>1,564</td>
</tr>
<tr>
<td>35 + 1</td>
<td>87</td>
<td>318.3</td>
<td>319.9</td>
<td>63</td>
<td>2,548</td>
</tr>
<tr>
<td>37 + 4</td>
<td>91</td>
<td>322</td>
<td>342.3</td>
<td>67</td>
<td>3,025</td>
</tr>
</tbody>
</table>

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A recent cohort-study has found a relative risk of 8.3% of major malformations associated with GLP-1RA in pregnant women with type II diabetes [10]. But the cases that have been reported thus far, unintentional exposure to GLP-1RA during pregnancy did not seem to have an impact on short-term fetal outcomes. However, these case reports have limitation of small sample size. Furthermore, studies on pregnant animals have shown that GLP-1RA has a higher risk of early pregnancy loss and fetal weight loss. Based on current evidence-based medical evidence, GLP-1RA should be avoided during pregnancy [11]. In addition, women should use contraception while taking such medications, and plan pregnancy until at least 2–3 months after discontinuing drugs [12]. If accidentally exposure to GLP-1RA during pregnancy, it is advisable to immediately discontinue using and promptly consult a specialist to assess the potential risks they may pose to the developing fetus.

According to the current case reports, accidental exposure to GLP-1RA during pregnancy does not appear to be an absolute indication for termination of pregnancy. It is recommended that pregnant women undergo regular prenatal examinations, closely monitor fetal bone development and weight gain through ultrasound.

Table 2 Summary of research studies on the maternal and fetal outcomes of being exposed to GLP-1RA in early pregnancy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Drugs of exposure</th>
<th>Last administration</th>
<th>Pregnancy outcomes</th>
<th>Mode of delivery, gestational age of delivery</th>
<th>Indication of cesarean section</th>
<th>Neonatal complications</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semaglutide and pregnancy [4]</td>
<td>PCOS</td>
<td>Semaglutide (0.5–1.0 mg/w)</td>
<td>GW 3 + 4</td>
<td>Delivered a healthy infant</td>
<td>Delivered a healthy infant</td>
<td>Hypoglycemia</td>
<td>At 6 months, the child developed normally</td>
</tr>
<tr>
<td>A case report of a pregnant woman with type 2 diabetes mellitus using dulaglutide during the first trimester of pregnancy [8]</td>
<td>T2DM</td>
<td>Dulaglutide (1.5 mg/w)</td>
<td>GW 13</td>
<td>Delivered a healthy infant</td>
<td>By cesarean section (GW 38 + 4)</td>
<td>Mild bilateral renal pylectasis</td>
<td>/</td>
</tr>
<tr>
<td>Case report: exenatide use during pregnancy [9]</td>
<td>T2DM</td>
<td>Exenatide (1.8 mg/d)</td>
<td>GW 14</td>
<td>Delivered a healthy infant</td>
<td>By cesarean section (GW 38)</td>
<td>Fetal intolerance of labor</td>
<td>At 2 months revealed normal weight and neuro-development</td>
</tr>
<tr>
<td>Normal pregnancy outcome after first-trimester exposure to liraglutide in a woman with Type 2 diabetes [5]</td>
<td>T2DM</td>
<td>Liraglutide (1.8 mg/d)</td>
<td>GW 13</td>
<td>Delivered a healthy infant</td>
<td>By cesarean section (GW 37)</td>
<td>/</td>
<td>No developmental abnormalities were found at 3 months</td>
</tr>
<tr>
<td>Liraglutide administration improves hormonal/metabolic profile and reproductive features in women with HAIR-AN syndrome [6]</td>
<td>HAIR-AN syndrome</td>
<td>Liraglutide (1.8 mg/d)</td>
<td>/</td>
<td>Delivered a healthy infant</td>
<td>/</td>
<td>/</td>
<td>None</td>
</tr>
<tr>
<td>Pregnancy outcome and liraglutide levels in serum and umbilical vein blood of a woman with type 2 diabetes [7]</td>
<td>T2DM</td>
<td>Liraglutide (1.8 mg/d)</td>
<td>GW 39</td>
<td>Delivered a healthy child</td>
<td>By cesarean section (GW 39)</td>
<td>/</td>
<td>None</td>
</tr>
</tbody>
</table>

GLP-1RA, glucagon-like peptide-1 receptor agonist; PCOS, polycystic ovary syndrome; HAIR-AN, hyperandrogenism-insulin resistance-acanthosis nigricans; T2DM, Type 2 Diabetes Mellitus; GW, gestational week.
In addition, it is also important to provide informed consent to patients. But the safety of GLP-1RA exposure during pregnancy still requires further confirmation through clinical studies. This report may contribute to enhance our understanding of the limited data regarding human exposure to semaglutide in pregnant women.

Maternal overweight and obesity prior to conception not only increase the risk of infertility and complications throughout pregnancy and the perinatal period, but also have detrimental effects on offspring’s growth and development. Therefore, it is crucial to improve preconception weight management as well as monitor weight gain during pregnancy [13]. Semaglutide is the preferred drug for weight loss and has become a new favorite for women of childbearing age. The woman who takes semaglutide should also learn about the contraindications to the medications. Furthermore, should be educated if they plan a pregnancy to only use safe and well studied medications for pregnancy and the fetus before getting pregnant [14, 15].

Conclusion
Following up until the age of 6 months, the child was developing normally. Although the current normal pregnancy outcome, does not provide sufficient evidence to determine the safety of semaglutide using during pregnancy. The safety of GLP-1RA in pregnant women has not been established and needs to be further confirmed by more clinical studies. More data are needed to assess its safety.

References