OBESITY IN PREGNANCY

Alexa Letizia
Montefiore OBGYN AI

OVERVIEW

Definition + Pathophysiology

Risks

- Prenatal
- Intrapartum
- Postpartum

Management

- Pregnancy
- Postpartum

GLP-1 RA

OBESITY

BMI Categories:

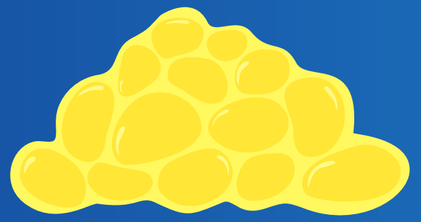
<18.5	18.5-24.9	25-29.9	30-34.5	35-39.9	>40
Underweight	Normal	Overweight	Class I Obesity	Class II Obesity	Class III Obesity

12.4%[2]

Among women aged 20-39:

39.7%[1]

PATHOPHYSIOLOGY



Active endocrine organ

Metabolic and inflammatory dysfunction

Chronic hypertension, cardiovascular disease, type 2 diabetes, sleep apnea, NAFLD[6]

+

Intrapartum

Antepartum

Postpartum

Maternal + Fetal Sequelae

RISKS ASSOCIATED WITH OBESITY IN PREGNANCY

EARLY PREGNANCY

- Spontaneous Abortion (OR 1.2)[3]
- Recurrent Pregnancy Loss (OR 3.5)[3]
- Congenital Anomalies[6]
  - Neural tube defect
  - Hydrocephaly
  - Cardiac
  - Orofacial
  - Limb reduction

Limitations of US: 20% less likely to detect anomalies[5]

GESTATIONAL DIABETES

- Insulin resistance[7]

30-34.5	35-39.9	>40
Class I Obesity	Class II Obesity	Class III Obesity
3x ↑	4x ↑	6x ↑

PREECLAMPSIA

- Proinflammatory → antiangiogenic factors[11]
- More than six times as likely than normal BMI
  - Risk doubles with each 5-7 kg/m^2 increase in pre-pregnancy BMI[9]

18.5-24.9	30-34.5	35-39.9	>40
Normal	Class I Obesity	Class II Obesity	Class III Obesity
3.4%	10%	12.8%	16.3%[9]

FETUS

- Birth timing
  - 30% increase in medically indicated preterm birth[12]
    - Unclear affect on spontaneous preterm birth
  - Higher likelihood of postterm pregnancy[13]

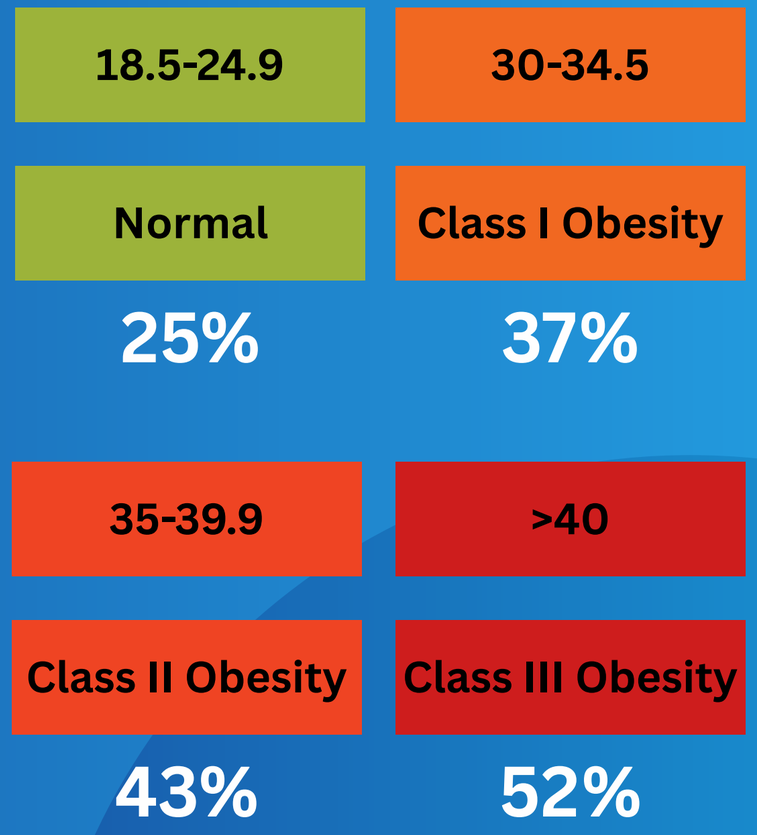
- Size
  - LGA and SD even after controlling for GDM[14]
  - FGR[14]

- Increased risk of PPROM[10]

- Increased perinatal mortality[12]
  - Stillbirth and neonatal death

DELIVERY

- Increased need for induction
  - 2x as likely to have failed IOL[16]
- Longer first stage, not second[15]
- Higher likelihood of Cesarean section
  - Partially accounted for by complications
- 2x as likely to fail TOLAC[18]
  - 2x maternal morbidity and 5x neonatal injury[19]
- Anesthesia and analgesia
  - Epidural/spinal failure
  - Difficult intubation[20]



POSTPARTUM

- Higher risk of hemorrhage secondary to atony
  - Vaginal delivery, not CS[21]
- 2-4x odds CS wound infection and dehiscence[22]
  - 30% if BMI>50, most diagnosed after discharge
- Venous thromboembolism[23]
- 30% increased likelihood of postpartum depression[24]

LONG-TERM EFFECTS ON CHILD

- Increased risk of
  - Childhood metabolic syndrome and obesity
    - One parent 2-3x[25]
    - Both parents up to 15x[26]
  - Asthma[25]
  - Behavioral disorders[25]
  - Developmental delay[25]
  - ADHD[25]

MANAGEMENT OF OBESITY IN PREGNANCY

PRENATAL

1st trimester

- A1c
- Screen for OSA
- cfDNA
  - Lower fetal fraction[27]
- Evaluate for nutritional deficiencies: iron, folate, vitamin B12, calcium, and vitamin D
- At least 0.4 mg, consider up to 5 mg, of folic acid supplementation
- Low dose aspirin <12wks if 2+ PEC risk factors[28]

Dietitian consultation

- Nutrient-dense foods
  - Higher amounts of fruit, vegetables, whole grains, nuts, seeds, legumes
- Lower intakes of red meat, processed and fried foods[8]

Exercise

- At least 150 minutes of moderate physical activity per week
  - Some recommend 30–60 minutes of moderate physical activity per day for those with obesity[8]

PRENATAL

Institute of Medicine weight guidelines endorsed by ACOG

- No distinction between classes of obesity

- Data is mixed
  - Some studies suggest no harm with more restrictive weight gain limitations[29]
  - Other research points to the guidelines as too restrictive
    - Increased preterm, SGA, perinatal mortality
    - Decreased LGA, need for CS[30]

Table 4. Recommendations for Total and Rate o Body Mass Index

Prepregnancy Weight Category	Body Mass Index*	Recommended Range of Total Weight Gain (lb)
Underweight	Less than 18.5	28–40
Normal weight	18.5–24.9	25–35
Overweight	25–29.9	15–25
Obese (includes all classes)	30 and greater	11–20

PRENATAL

2nd trimester

- Anatomy scan
- GDM screening
  - Early at 18-20 weeks
    - If negative, repeat at 24–28 weeks

3rd Trimester

- Fetal growth[33]
  - After 28 weeks, consider fetal growth assessment every four to six weeks
  - Prepregnancy BMI of 35.0–39.9
    - Consider weekly antenatal surveillance at 37 weeks
  - Prepregnancy BMI >40
    - Consider weekly antenatal surveillance at 34 weeks

LABOR AND DELIVERY

- Route for standard obstetric indication
- Consider equipment needs
  - Beds, fetal monitoring, BP cuffs, OR equipment
- Timing
  - One protocol:[34]
    - Delivery by due date if:
      - Prepregnancy BMI ≥40
      - Prepregnancy BMI 35 to 39.9 plus GDM or LGA fetus
      - Prepregnancy BMI 30 to 34.9 plus GDM and LGA fetus
    - 10.8% reduction in CS, but stillbirth rates did not change
  - A retrospective cohort study[35]
    - Induction at 39 or 40 weeks → 20% decrease in CS and 40-70% decrease in macrosomia
    - Nonstatistically significant trend toward fewer infant deaths

CESAREAN CONSIDERATIONS

Antibiotic Prophylaxis

- Based on general surgery data[36]:
  - 2g prophylactic cefazolin if >80 kg
  - 3g if >120 kg

Thromboprophylaxis

- Lovenox 40mg daily after CS
- Consider risk factors after vaginal delivery[23]

Wound Closure

- Closure of subcutaneous tissue with a depth >2 cm significantly decreases the incidence of wound disruption[37]
- Limited data on special wound dressing
- Prophylactic negative pressure wound therapy may decrease infection but not dehiscence
  - May increase complications[38]

PRECONCEPTION

WEIGHT LOSS BEFORE CONCEPTION

- Even small reductions are beneficial
  - 5–7% reduction can significantly improve metabolic health[39]
  - 10% reduction reduces risk of preeclampsia, gestational diabetes, indicated preterm birth, large for gestational age (LGA)/macrosomia, and stillbirth by 10 percent
  - 20 to 30% reduction reduces risks of cesarean birth and shoulder dystocia[40]
- Use motivational interviewing techniques
  - Individualized, patient-centered approach toward exploring and resolving ambivalence

WEIGHT LOSS MEDICATIONS

- Anorectics that suppress appetite and pancreatic lipase inhibitors
  - Not recommended due to safety concerns and adverse side effects[41]

- Metformin for obese pregnant patients started at 10-20 weeks does not improve pregnancy or birth outcomes[42]

GLP1-RAs?

NEW CONCERNS: GLP1S

Increasing prevalence of obesity

Increasing use of GLP1s

50% of pregnancies are unplanned

Increasing chance of potential incidental exposure

GLUCAGON-LIKE PEPTIDE-1 (GLP1) AGONISTS

- Widely used for T2DM, recently gained approval and popularity for obesity

- Short acting: Exenatide, lixisenatide and beinaglutide
- Long acting: Dulaglutide, semaglutide, liraglutide and albiglutide

- High molecular weight
  - Not likely to passively cross placenta and minimizes the risk of direct fetal exposure

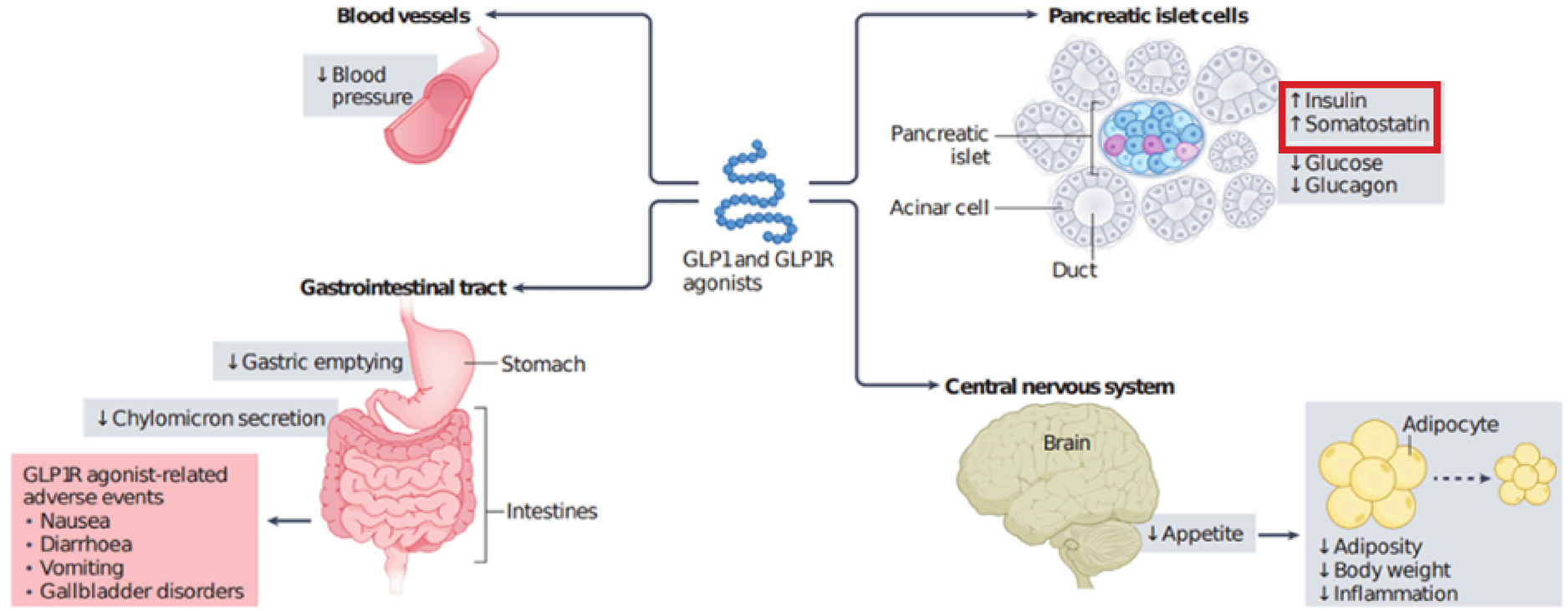
- Likely low excretion in breast milk then digested by fetus[43]

- Effects on maternal metabolism may affect fetus

MECHANISM

Endogenous incretin hormone secreted by L-cells of the small intestine in response to food intake

FIGURE
Mechanisms of glucagon-like peptide-1 receptor agonists throughout the body



Adapted from Ussher and Drucker.[28]
Reproduced with permission from Ussher and Drucker.[28]

ANIMAL STUDIES

Briggs et al., 2011[44]

- Rats and rabbits exposed to high doses of liraglutide had various fetal malformations at all doses
- Reduction in fetal growth in doses below expected in humans

Muller et al., 2023[45]

- Systematic review 23 studies of GLP-1 RAs during pregnancy and nursing in animals
- Decreased fetal weight and growth, delayed ossification, skeletal variants, and visceral anomalies
- Increase in embryonic death

CASE REPORTS

- ~10 case reports published in the literature of pregnancies with inadvertent exposure to GLP-1RA during pregnancy[46]
  - Variable times of exposure
  - Anomalies: mild bilateral renal pyelectasis, ASD
  - Neonatal hypoglycemia

PROSPECTIVE COHORTS

Cesta et al., 2023[47]

- Multinational study of 51,826 pregnant patients with T2DM and their infants
- Prevalence of major congenital malformations similar in infants with periconceptional GLP1-RA exposure (n=938) compared to those on insulin
- No increased risk of major congenital malformations

Dao et al, 2024[48]

- Multinational study of 168 pregnant women exposed to a GLP1-RA during the first trimester of pregnancy
- Major birth defects in GLP1-RA-exposed women reference group and population rate
- No identified pattern of birth defects

IN SUM

FDA

- Stop GLP-1 RA ideally two months before becoming pregnant or as pregnancy is discovered

ACOG

- Studies do not suggest strong teratogenic effects, further research needed
- Balance risk of continuing GLP-1RA until confirmation of pregnancy vs. prematurely stopping these medications and risking reversal of glycemic control /weight loss

RESOURCES

ACOG Practice Bulletin: Obesity in Pregnancy

Management of Prepregnancy, Pregnancy, and Postpartum obesity from the FIGO Pregnancy and Non-Communicable Diseases Committee

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Thank you!

Any questions?