Review

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Maternal obesity: Perinatal implications

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Abstract

Over the previous three decades, the prevalence and growth of overweight and obese status has risen relentlessly in both the general population and pregnant women. This rise is seen in both higher pre-pregnancy body mass index measurements along with excessive weight gain during pregnancy. Maternal obesity has been shown to exacerbate co-morbidities such as insulin resistance, pregnancy induced hypertension, and infectious states in parturient mothers. These changes have been shown to subsequently increase rates of fetal anomalies and affect fetal growth, as well as various aspects of the delivery such as rates of instrumented vaginal deliveries and an increase in delivery by cesarean section. Maternal obesity increases fetal birth weight, influences the delivery room resuscitation of the neonate by increasing the need for respiratory support, and increases the risk of neonatal hypoxic ischemic encephalopathy. This review also looks at recent studies revealing the strong association between maternal and offspring obesity and other long-term neurodevelopmental outcomes of offspring.

Keywords

Obstetrics/gynecology, women's health, pregnancy, obesity, maternal obesity, neonatal outcomes

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Introduction

The global obesity epidemic has contributed to increased burden of obesity during pregnancy and worsening perinatal outcomes. Globally, prevalence of obesity in women has increased from 6.4% in 1975 to 14.9% in 2014.[1] High-income countries, including the United States, have historically had the highest rates of obesity worldwide.[2] In 2009, National Health and Nutrition Examination Survey found the prevalence of obesity in US women aged 20–39 to be 31.9% with a notably higher prevalence of 56.2% in non-Hispanic Black women.[3] The burden of maternal obesity is also increasing in middle-income countries with the largest populations of obese pregnant women living in India, China, and Nigeria.[2] Worldwide, there were an estimated 14.6 million obese pregnant women in 2014.[2]

Obesity is evaluated using body mass index (BMI) which is calculated by dividing weight in kilograms by the square of height in meters and is defined as BMI $\geqslant$30 kg/m^2.[4,5] Class I obesity includes BMI 30–34.9, class II obesity is BMI 35–39.9, and class III obesity is defined as BMI $\geqslant$40.[4,5] Many studies also assess outcomes for superobese individuals who have BMI of $\geqslant$50.[6]

Maternal obesity has negative effects on the mother and fetus both during pregnancy and delivery, as well as on the offspring during the neonatal period and later in life. There is a growing body of research on interventions aimed to reducing these risks, with the most successful approach being reducing maternal obesity prior to conception. The topics covered in this review are summarized in Figure 1.

Body

Methods

This review includes studies from PubMed and national guidelines available online that were published in or translated to English. Publications were also selected by reviewing reference lists of recent published articles. Observational studies, meta-analyses, and review articles were included, though effort was taken to find and individually review primary studies cited by meta-analyses. Keywords for searches included "maternal obesity," "obesity in pregnancy," and "fetal outcomes of obesity in pregnancy." Focus was placed

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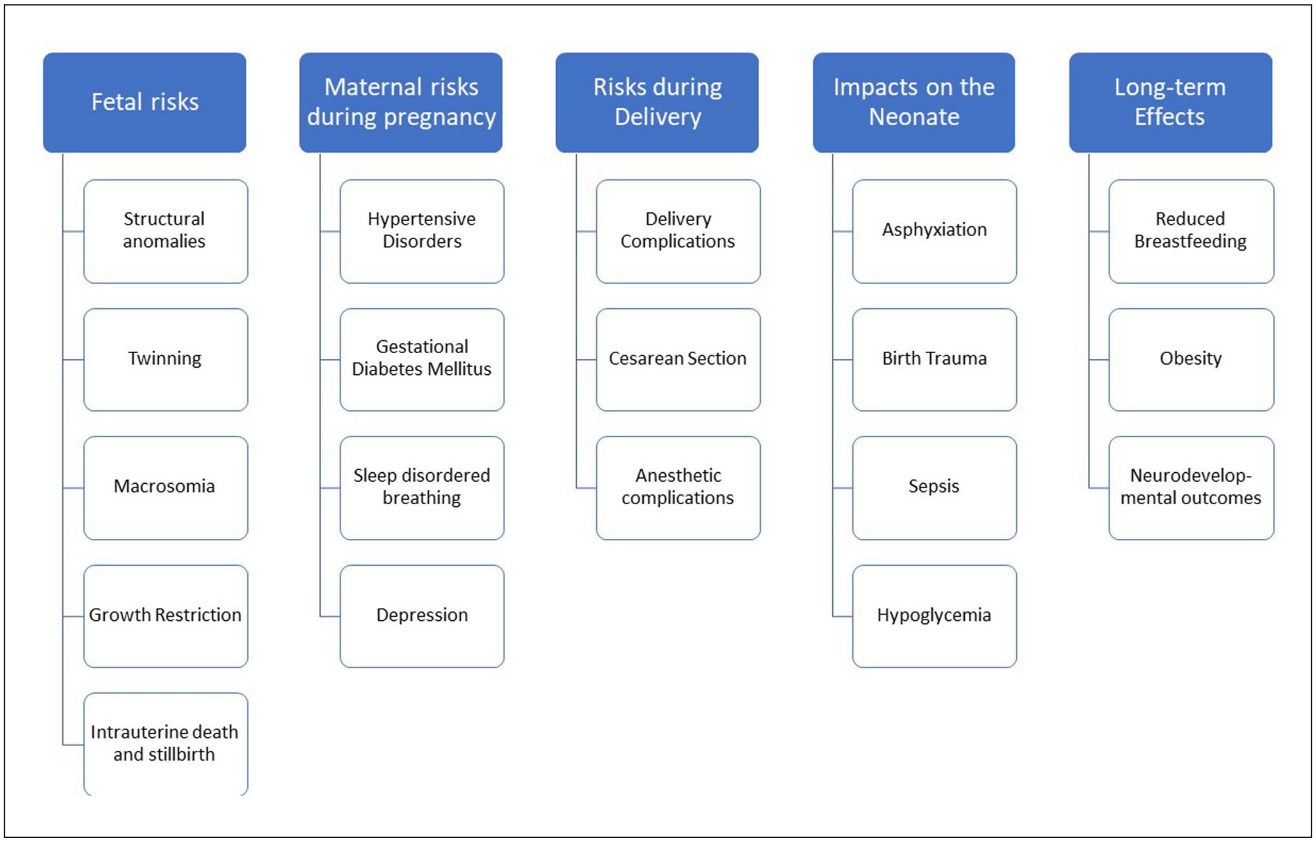

Figure 1. Summary of perinatal outcomes associated with maternal obesity.

on articles that specifically included outcomes experienced by the fetus/offspring affected by maternal obesity, not just outcomes affecting the mother. One author performed initial search, and both remaining authors were involved in secondary review of the articles. Date of publication was not a limiting factor, although emphasis was placed on articles published after 2005. As this paper reviews a heterogeneous mix of outcomes and effect measures, it is limited in its ability to directly compare study results.

Impact of maternal obesity on the fetus

Worldwide data show that maternal obesity is associated with a significantly higher risk of fetal complications related to an increase in fetal structural abnormalities and multiple gestation. It has also been associated with stillbirth, preterm birth, fetal growth restriction (FGR), and macrosomia. These risks can occur independently or in concert with each other, further increasing the risks to the fetus and neonate.

Structural fetal anomalies. In a 2009 systemic review, fetal abnormalities were analyzed in overweight and obese women, in comparison to average weight women.[7] They showed that the incidence of fetal anomalies increases with increasing maternal BMI, and effects were greater in multiple gestations.[8] A similar result was also seen in recent Swedish population-based study: as maternal BMI increased, the incidence of fetal abnormalities progressively increased.[9] The overall rate of major organ malformations increased from 3.5% in normal weight mothers, to 4.7% with class III obesity.

Structural fetal defects reported to be significantly associated with maternal obesity include malformations in the central nervous system, cardiac structures, digestive systems, limbs, and genital organs. In a meta-analysis, maternal obesity was associated with neural tube defects (NTDs), cardiovascular anomalies, orofacial clefts, and other anomalies.[7] The largest risk was reported in the nervous system, with an adjusted risk ratio of 1.15 in overweight women compared to 1.88 in women with class III obesity.[9] Studies specific to NTDs have found that women with BMI $\geqslant 30$ are almost twice as likely to have a fetus with NTD compared to the non-obese and there is a dose–response relationship with increasing maternal obesity.[10,11]

High maternal BMI was also associated with fetal cardiac abnormalities, which accounted for a third of all the severe fetal structural abnormalities. The adjusted risk ratios ranged from 1.05 in the overweight to 1.44 in class III obese women, with higher risks seen in male babies.[9] In a population cohort study, the incidence of congenital heart defect was 1.4% in the entire population, and included complex defects such as tetralogy of Fallot, transposition of the great arteries, atrial septal defects, aortic arch defects, and single ventricle hearts. Cardiac defects were reported to be more severe in women with BMI $\geqslant 35\,kg/m^2$, including a nearly doubled risk of aortic arch defects and transposition of the great arteries, while occurrences of less severe defects such as atrial septal defect and patent ductus arteriosus were noted to increase with increasing maternal BMI.[12]

Maternal obesity is also associated with higher risks for other structural defects such as orofacial cleft, cleft lip or palate, and congenital renal and urinary tract abnormalities.[13,14] Many of these defects develop during the period of organogenesis that occurs in the first 8 weeks of pregnancy, suggesting that maternal weight should be optimized prior to conception.[9]

Maternal BMI complicates detection of structural abnormalities by antenatal ultrasound.[15,16] Incomplete fetal anatomical examinations are reported to be more common in obese mothers, ranging from 10.2% in normal weight mothers to 44.1% in mothers with class III obesity. The image quality is reported as suboptimal more frequently in correlation with maternal obesity, particularly with fetal chest and cardiac system.[16] Aneuploidy soft markers, such as increased nuchal fold, may also go undetected.[17]

Twinning. The overall rates of dizygotic twinning have increased worldwide over the last half century.[18] This increase has largely been attributed to the use of assisted reproduction methods; however, it is also now thought to be associated with the increase seen in maternal obesity.[19] Data from the Collaborative Perinatal Project found that as the maternal weight increased, there was a significant increase in naturally occurring dizygotic twinning in women with BMI $\geqslant 30\,kg/m^2$. These are pregnancies conceived without help of fertility medications. Monozygotic twinning is unaffected by maternal BMI.[19,20]

Multiple gestations are known to independently increase maternal and perinatal risks. Twin gestations further increase risk for complications already known to be more prevalent in obese women, such as gestational diabetes, gestational hypertension, and preeclampsia.[8,21,22]

Fetal macrosomia and growth restriction. It is well established that fetal macrosomia at birth is associated with risks which include an increased risk of intrauterine fetal death (IUFD), abnormalities in labor, fetal hypoxia, higher operative deliveries and related complications, shoulder dystocia, as well as neonatal risks which include hypoglycemia, hyperbilirubinemia, and higher need for care in the neonatal intensive care.[23]

Association of maternal obesity with macrosomia was documented with data from the regional Maternal Information System database consisting of 350,311 completed singleton pregnancies.[24] A 2008 literature review identified modifiable and non-modifiable risk factors, including maternal pre-pregnancy BMI, weight gain during pregnancy, overall nutrition, and level of physical activity.[23] A recent meta-analysis of 16 observational studies identified pre-pregnancy maternal BMI of $\geqslant 30\,kg/m^2$ as a significant risk factor of fetal macrosomia, in both nulliparous and multiparous patients.[25–27] Gestational diabetes is also an independent factor for fetal macrosomia. Furthermore, maternal obesity and gestational diabetes are commonly associated with increased rates of labor induction and cesarean section, which compound neonatal risks, especially for the macrosomic neonate.[28]

FGR is also seen more frequently in association with maternal obesity.[29] Compared to non-obese women, obese women are more likely to develop severe FGR as well as abnormal umbilical artery flow.[30] These babies are at increased risk for stillbirth, preterm delivery, and perinatal asphyxia. FGR also has long-term consequences which are considered to be a result of epigenetic changes that can lead to metabolic consequences.[31]

Maternal obesity complicates the ultrasound assessment of fetal growth in singleton and twin pregnancies. The positive predictive value for diagnosis of fetal macrosomia as well as FGR is low, though the negative predictive value is high.[32] Closer to the time of delivery, in twin gestations, ultrasound assessment of fetal growth appears to be more reliable.[33]

Intrauterine fetal death and stillbirths. Evidence suggests that pre-pregnancy maternal obesity is associated with an increase in the risk of late fetal death. The most significant risks are seen in high BMI nulliparous mothers, in whom the risk for neonatal deaths is more than doubled.[34,35] These risks are independent of structural defects or diabetes. Though preeclampsia was noted to be more common in women that experienced IUFD, even when preeclampsia was excluded, the risk of IUFD was documented to be increased in the obese women.[7]

In a meta-analysis of 38 studies, even a modest increase in the maternal pre-pregnancy BMI was associated with an increase in fetal and neonatal deaths. The relationship was linear, with higher numbers of fetal deaths seen in women with higher BMI. In women with a BMI of 40 the risk was increased two to three fold.[36] In an autopsy-based study, the deaths can occur before and after 24 weeks, and are more common in the macrosomic fetus.[37,38]

Impacts of maternal obesity on mothers during pregnancy

Obesity significantly increases the mother's risk of comorbidities during the pregnancy and the perinatal period. Notably, there is a dose–response relationship of comorbidities and increasing BMI.

Hypertensive disorders and gestational diabetes mellitus. In a recent meta-analysis, obese women were found to be at significantly increased risk for hypertensive disorders of pregnancy and gestational diabetes mellitus (GDM) compared to women with normal BMIs.[39] Hypertensive disorders of pregnancy include chronic hypertension, gestational hypertension with onset after 20 weeks' gestation, and preeclampsia.[40] Overweight and obese women are at higher risk of both preexisting hypertension and diabetes as well as developing the conditions during pregnancy.[39] Women with class I obesity had a prevalence of 15.9% for hypertensive disorders and 17.0% for GDM, compared to 3.5% and 3.9% respectively for women of normal BMIs.[39] A Canadian cohort of women with super obesity demonstrated even higher rates of comorbidities including a 19.7% prevalence of gestational hypertension and 21.1% prevalence of GDM.[41] A birth cohort in Missouri similarly reported an increasing risk of preeclampsia—ranging from 7.4% in class I obesity to 13% in super obesity (defined as BMI $\geqslant 50\,kg/m^2$).[42] In a systematic review of complications in obese mothers, obesity was associated with 3–10 times increased risk of preeclampsia and 4–8 times increased risk of gestational hypertension.[43]

Across the literature, systematic reviews and international cohort studies indicate a strong association between obesity and GDM.[39,43,35–37] Two systematic reviews found that when women are obese, their risk of GDM increases four to nine fold, and prevalence of GDM increased by 0.92% for every unit (kg/m^2) of BMI gained.[44,45] This can also have longer lasting effects, with development of type 2 diabetes later in life.[46,47]

Maternal complications can, in turn, have negative impacts on the health of the baby. Preeclampsia, especially with severe features, increases the risk of FGR, preterm delivery, risks associated with preterm delivery, as well as stillbirth and neonatal demise.[48] Preeclampsia has been shown to increase offspring's risk of obesity, diabetes, hypertension, and poor neurodevelopmental outcomes.[48–53]

Gestational diabetes is known to independently have a negative impact on the baby. Maternal hyperglycemia increases risk of fetal macrosomia and related complications during delivery, such as shoulder dystocia and other injuries.[47,54–58] Animal models and human cohort studies have found significant association between GDM and future risks for the offspring which include obesity as well as insulin resistance and development of type 2 diabetes.[46,54,59,60]

Sleep disordered breathing and depression. In addition to hypertensive disorders and diabetes, obesity has been associated with sleep-disordered breathing during pregnancy and depression. Sleep-disordered breathing increases risk for low birthweight, preterm birth, assisted vaginal deliveries, cesarean section, and neonatal intensive care unit (NICU) admissions.[61–63] The association with low birth weight may be neutralized in obese populations by the well-established association between obesity and fetal macrosomia. There is a growing body of evidence showing an association between perinatal depression and maternal obesity, which may affect the care an infant receives after birth.[43,64]

Impacts of maternal obesity on delivery

Obesity has negative effects on delivery outcomes, including increased complications with vaginal delivery as well as higher cesarean section rates. In addition, maternal obesity contributes to difficulties in use of epidural and general anesthesia for both vaginal and cesarean deliveries.

Delivery complications. Women with class I obesity have significantly lengthened first and second stages of labor, increased need and dosing of oxytocin, and higher incidence of second- or third-degree perineal tears.[65] The rate of hemorrhage during delivery was increased, and risk of sepsis following vaginal birth was reported to be more than 10 times as likely in obese women, but there was no significant impact on instrumental delivery.[66,67] Obese women that attempt trial of labor after cesarean (TOLAC) following a prior cesarean section had a higher rate of failure, and also had a greater than five-fold increase in risk of uterine rupture/dehiscence, a life-threatening risk associated with TOLAC.[68,69]

Cesarean section. There is a large body of evidence that obesity contributes to increased rates of cesarean section and subsequent impaired wound healing, and these risks increased with class of obesity.[39,41,42,65,70–72] The increased rate of cesarean delivery is due to failures in progress of labor as well as fetal distress.[67] Cesarean deliveries are known to have many risks, both intra- and post-operatively. While some studies suggest that intra-operative risks may be similar across all BMI classes, others have found that obesity is associated with longer surgical and anesthesia time, as well as higher rates of maternal admission to intensive care units.[73,74]

Anesthetic complications. Several studies have found that failure rates of epidural anesthesia and complications are significantly increased in obese patients.[67,75,76] Complications occurred both in the placement of epidural catheter, as well as an increased risk of dural puncture and subsequent headache. The use of epidural analgesics more frequently lead to persistent hypotension and prolonged fetal heart rate decelerations.[75,76] Use of general anesthesia in emergent cesarean deliveries in morbidly obese mothers was also associated with significant risks.[77] Complications in both vaginal and cesarean delivery may lead to additional issues in the postpartum period, such as inability to initiate breastfeeding, which will be discussed in a subsequent section.[78]

Impacts of maternal obesity on the neonate

Maternal obesity has a broad range of effects on her baby at and immediately following birth. In addition to the increased risk of delivery complications listed above, effects on the neonate include fetal acidosis, perinatal asphyxia, need for resuscitation and/or respiratory support, birth trauma, metabolic deviations, greater chance of NICU admission with increased length of stay, and an overall increased risk of stillbirth or death.

Infant asphyxiation. A series of studies done by a group in Sweden examined the impact of degree of maternal obesity on infant asphyxiation during birth and related morbidities. They have shown that incidence of asphyxia-related adverse outcomes and resultant low Apgar scores increased by as much as three fold in mothers with grade 3 obesity.[9] More recently they reported that maternal obesity correlates with increased rates of fetal acidosis resulting from prolonged oxygen deprivation during delivery.[79] They found that this association correlated with increased rates of cerebral palsy in children of obese mothers, most likely associated with asphyxia during birth.[80] Similar studies performed in Japan found that pre-pregnancy BMI and gestational weight gain both increased asphyxia-related neonatal morbidity.[81,82]

Birth trauma, sepsis, and hypoglycemia. Perinatal birth trauma, such as shoulder dystocia or injury to the peripheral nervous system or skeleton, is also more frequent in obese mothers. Infants born to mothers with class III obesity are 1.5–3 times as likely to have shoulder dystocia occur during birth than those born to non-obese mothers.[41,83] A large cohort study found infants born to overweight and obese mothers had a 50%–150% greater likelihood of a birth injury to the skeleton.[66] Relative risk of bacterial sepsis in the newborn was 2.90.[66,84] Incidence of birth asphyxia, feeding problems in the newborn, and hypoglycemia were also seen in offspring of obese mothers at rates two to three times those seen in normal weight mothers. Impact of maternal obesity on neonatal metabolism also shows a link between degree of maternal obesity and neonatal hypoglycemia, hypomagnesemia, and hypocalcemia.[41,66]

Many of these findings have been included in a 2019 meta-analysis which examined pregnancy outcomes by BMI.[39] This analysis included over 3.7 million pregnancies across 13 studies and found that babies were most at risk for hypoglycemia, macrosomia, infection, birth trauma, respiratory distress, death, and neonatal intensive care unit admission. When ranked by obesity category, they found that these risks increased with increasing maternal obesity. This and other studies indicate that rates of NICU admission increase with maternal obesity.[39,41,66]

A meta-analysis found that incremental increases of even 5 units in BMI, were associated with increased relative risks of fetal death, stillbirth, neonatal, perinatal, and infant death.[36] The most substantial increase in risk was seen in class III obese women, who had a two- to three-fold increase in the relative risk of these outcomes. Similar results have been found in more recent studies looking at obese women in specific geographical locations: Asia, Denmark, and the United States.[85–88] While the mechanisms for how maternal obesity contributes to fetal and neonatal death are not well understood, some studies suggest that they may be due to maternal hypertension, placental dysfunction, umbilical cord complications, intrapartum events (such as birth trauma, uterine rupture, or meconium aspiration), fetal abnormalities, and increased rate of infection in the mothers.[86,88,89]

Long-term effects of maternal obesity on the child

Breastfeeding. Maternal obesity is associated with life-long impacts on the health of her child. Obese women are as much as three times less likely to initiate breastfeeding and when they do, it is often for a shorter duration.[43,78,90–93] This has been attributed to elevated progesterone that may impair lactogenesis, larger breasts making latching difficult, or sociocultural and psychological reasons.[43] Lack of breastfeeding may deprive the child of the benefits of breastfeeding, which include reduction in childhood mortality incidence, and mortality from infectious diseases, as well as an increase in intelligence quotient points in childhood.[94–98] Breastfeeding is also reported to protect the child from obesity, type 2 diabetes, and asthma later in life.[99–102]

Obesity. Maternal obesity is an independent risk factor for obesity in the offspring, creating an intergenerational cycle.[90,103–107] The etiology of childhood obesity is complex, and the association remains after controlling for confounding factors including offspring lifestyle and socioeconomic status.[108–110] This suggests that maternal obesity alone, not its comorbidities, has a causative association with childhood obesity. Of note, none of these studies adjusted for maternal breastfeeding, so it is possible that this association is partially explained by decreased breastfeeding among obese mothers. GDM and hypertension have been associated with childhood obesity; however, after controlling for maternal obesity these associations were not found to be significant.[111]

The relationship between maternal and offspring obesity persists into adulthood.[109,110,112–114] Maternal obesity and associated complications in the offspring have been studied at age 32 and 62. An Israeli birth cohort contacted offspring at age 32 and found a strong association between elevated maternal and offspring BMI.[109] This study controlled for many factors including maternal socioeconomic status and education, maternal hypertension and GDM, as well as offspring physical activity, smoking, and education. Data from the Helsinki birth cohort found that maternal obesity was associated with offspring obesity and related complications such as cardiovascular disease, stroke, and diabetes at age 62 years.[110,113] These studies also controlled for socioeconomic status of mothers and offspring, as well as education and income of offspring. Similarly, data from a Scottish national cohort found that maternal obesity was associated with offspring admission for cardiovascular diseases and all-cause mortality.[114]

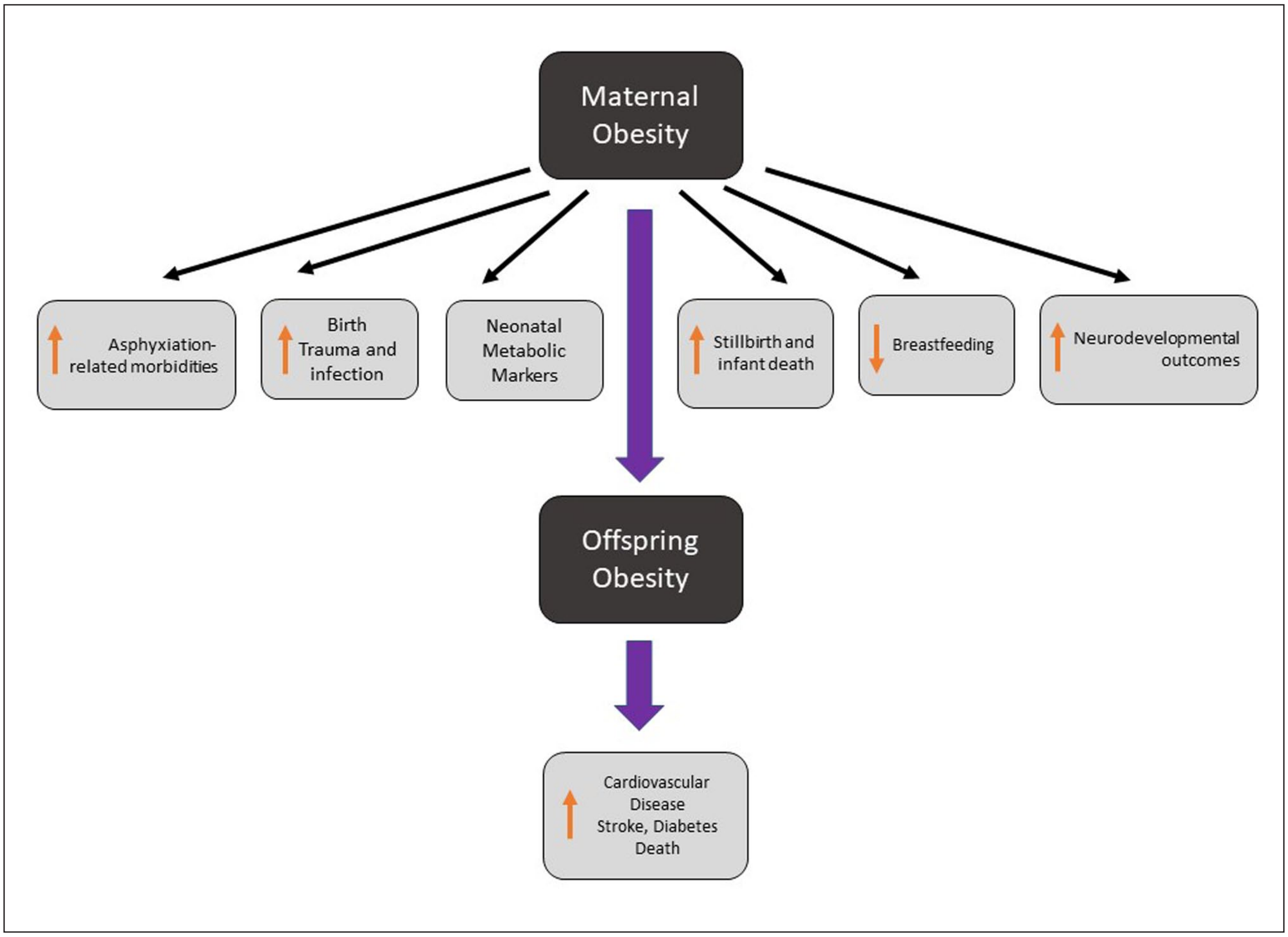

Figure 2. Long-term outcomes of offspring exposed to maternal obesity.

Neurodevelopmental outcomes. Systematic reviews have also found associations between maternal obesity and neurodevelopmental outcomes, specifically ADHD, autism spectrum disorder, developmental delay, emotional/behavioral problems, and general childhood cognitive development.[115,116] However, this research is limited by lack of standardized scales when measuring developmental outcomes and potential confounding by maternal intelligence, socioeconomic status, breastfeeding, maternal mental health, and postnatal lifestyle.

Effects of maternal obesity on the offspring at birth and long-term are summarized in Figure 2.

Limitations

This work represents a narrative review. It is therefore limited in scope and does not represent a comprehensive review of the subject matter. The authors did not systematically review the literature, nor were there any direct comparisons between studies. Therefore, the material included, and the conclusions drawn, are subjective in nature, non-comprehensive, and are subject to the bias of the authors.

Conclusion

Elevated BMI and obesity are on the rise in women of reproductive age. Maternal obesity is associated with increased fetal and maternal risks, and the rise is incremental with increasing maternal BMI. Fetal risks include an increase in structural abnormalities, affecting multiple organ systems with the CNS and cardiac structures being the most impacted. The rate of multiple gestation, specifically dizygotic twins is also higher in women with BMI $\geqslant 30\,kg/m^2$. Fetal growth, macrosomia, FGR, fetal death, and stillbirths occur at higher rates in this population as well.

Maternal risks include higher complications during pregnancy, including gestational diabetes, hypertensive diseases of pregnancy, and higher incidence of cesarean section with higher peri-operative complications. The neonate is at higher risk for birth trauma, hypoxic insult and compromised respiratory function at birth, requiring admission to the NICU. The offspring of obese mothers are at higher future risks that include childhood obesity and related health problems into adulthood that include cardiovascular diseases, diabetes mellitus, and stroke.

Author contributions

JR, SC, and AR all contributed to the writing of this article. JR was responsible for review and editing. All authors reviewed and approved the final manuscript.

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