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Research Article

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Maternal and Long-Term Offspring Outcomes of Obesity during Pregnancy

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Abstract

Background and purpose: Obesity's prevalence is rising in women of reproductive age worldwide and has become the most common medical condition at this age group. Besides, its occurrence is also rising during pregnancy. This condition not only increases the risk of noncommunicable diseases on the mother, such as cardiovascular disease and diabetes, but also transfers this risk to the offspring.

Methods: This is a narrative review based on scientific and review articles on the matter.

Results: Obesity is associated with an increased risk of gestational diabetes mellitus, gestational hypertension and preeclampsia, venous thromboembolism, infection, and mental health problems. Furthermore, it has an impact on the progress of labor and induction matters. Regarding offspring outcomes, it is related to higher incidence of congenital anomalies, perinatal mortality, and the occurrence of large for gestational age newborns. Still, it has implications on cardiometabolic risk and neurodevelopment in offspring.

Conclusions: It is therefore imperative to encourage the adoption of healthy lifestyles, especially in the peri-conception and interpregnancy periods. Likewise, there must be support in the multidisciplinary monitoring of these pregnant women to minimize associated complication rates.

Keywords

Pregnancy, Maternal obesity, Risk management, Offspring

Introduction

Obesity's prevalence is rising in women of reproductive age worldwide and has become the most common medical condition at this age group [1,2]. By 2025, more than 21% of women will be obese [3]. Besides, its occurrence is also rising during pregnancy: from 9-10% in the early 1990s to 16-19% in the 2000s [4].

It is classified according to a person's body mass index (BMI), which is calculated according to the formula: Weight (in Kg)/height^2 (in meters) and expressed in Kg/m^2. Is an anthropometric measurement used to define people as underweight, normal weight, overweight and obese [5] - Supplementary Table 1. This standard classification for the nonpregnant population does not adapt well to pregnant women since their weight is supposed to rise over a relatively short interval of time and much of the weight gain is related to the fetus, placenta, amniotic fluid and increased blood and extravascular fluid volume. However, since no standard pregnancy-specific definition of obesity exists, pre-pregnancy BMI is utilized to classify pregnant women as obese or nonobese.

This condition not only increases the risk of noncommunicable diseases (NCDs) on the mother, such as cardiovascular disease and diabetes, but also transfers this risk to the offspring through sociocultural factors and epigenetic mechanisms [6-13]. For example, children born from mothers with obesity have an increased risk of poor cognitive performance and neurodevelopment disorders during childhood [9]. Furthermore, the risks are amplified with increasing severity of the condition [13-15].

The preconception period is a good opportunistic time for women with obesity to assess and manage conditions that

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Supplementary Table 1: Classification of body mass index.

Classification	BMI (Kg/m²)
Under weight	< 18.5
Normal weight	18.5-24.9
Over weight	25-29.9
Obesity	
Class 1	30-34.9
Class 2	35-39.9
Class 3	≥ 40

Adapted from World Health Organization, 2000 [5].

Abbreviations: BMI: Body Mass Index.

could influence their health and to optimize their weight before pregnancy [10,16-22]. Thereby, weight management strategies should ideally be implemented prior to pregnancy and can include dietary, exercise, medical and surgical approaches, with the first two strategies being the mainstay of weight management [23].

Although this preconception care is the ideal scenario, many women present to a doctor´s appointment already pregnant and they should be given the opportunity to discuss potential risks and management options during pregnancy [16].

Particular attention should be given for women with previous bariatric surgery, since they are at particular risk for nutritional deficiencies and fetal growth changes [16,23].

The main objective of this review is to identify and characterize core maternal and fetal complications associated with pregnant women with obesity.

Methods

This is a narrative review based on scientific and review articles on the matter, obtained from Pubmed®, using the *Medical Subject Headings* "pregnancy" and "obesity", having also resorted to books on the specialty of Obstetrics whenever the authors found it necessary.

Results

Maternal outcomes

Gestational Diabetes Mellitus (GDM): The prevalence of this disorder is significantly higher in pregnant women with obesity when compared with the general obstetric population (between 6-12%) and is supposed to be related to an increase in insulin resistance [24-26]. Besides this risk increases with rising maternal weight and BMI (one review showed an increase of 0.92% for every 1 Kg/m² in BMI) [27].

Gestational hypertension and preeclampsia: A 2003 systematic review demonstrated that the risk of preeclampsia doubled with each 5-7 Kg/m² increase in pre-pregnancy BMI [28]. The mechanism behind this is still not well understood, but it seems to follow the pathophysiologic changes associated with obesity-related cardiovascular risk, namely insulin resistance, a state of systemic inflammation and oxidative stress [29-32]. Furthermore, adipose tissue is also rich in proinflammatory cytokines, which can then promote the expression of maternal antiangiogenic factors implicated in the pathogenesis of preeclampsia.

Preterm birth: Obesity has proven to increase the risk of medically indicated preterm birth related to obesity-related maternal disorders (relative risk [RR] 1.3, 95% CI 1.23-1.37) [33]. On the other hand, it is less clear that it rises the risk of spontaneous preterm birth [34].

Progress of labor and induction issues: There seems to be an impact of maternal obesity on labor progression, with longer first stages of labor, that is usually independent of fetal size [35,36]. Kominiarek, et al., carried out a retrospective analysis on labor progression in about 119000 women. They established median times for nulliparous women to dilate from 4 to 10 cm of 5.4, 6, 6.7 and 7.7 hours at BMI < 25, 30-34.9, 35-39.9 and ≥ 40, respectively, after adjustment for confounders; a similar pattern was noted in parous women [37].

Besides, pregnant women with obesity are also at increased risk for longer inductions of labor (0.3 hours increase for each 10 kg increment in weight), induction failure (twice the risk) and both planned and intrapartum caesarean birth [38-40]. This last is usually related to higher infant birth weight, increased frequency of pre and post term birth and to obesity-related pregnancy complications [41,42].

Observational studies have also reported that a trial of labor after caesarean birth (TOLAC) is less likely to result in vaginal birth in pregnant women with obesity (failed TOLAC rate of 15% in normal BMI pregnant women versus 30% in pregnant women with obesity) [43].

Postpartum hemorrhage (PPH): Heslehurst, et al., demonstrated an increased risk of PPH in pregnant women with obesity that would not be surprising since obesity is associated with other risk factors for PPH, such as macrosomia, induced labor, caesarean birth) [44]. In the other hand, another meta-analysis did not prove this effect [45].

Venous thromboembolism (VTE): Obesity is an independent risk factor for VTE [46]; in one review, the odds of postpartum VTE in patients with class 1, 2 and 3 obesity were OR 2.5, 2.9 and 4.6, respectively when compared to women with normal BMI, with the risk of pulmonary emboli being greater than for deep vein thrombosis [47].

Infection: Pregnant women with obesity are at higher risk for postpartum infection (either wound infection or endometritis), regardless of mode of delivery and the use of prophylactic antibiotics (adjusted OR 2.24, 99% CI 1.91-2.64) [27,48]. This seems to be due to the higher risk in forming hematomas and seromas and the poorer vascularity of the subcutaneous adipose tissue.

Mental health problems: Obesity is associated with an increased risk for postpartum depression (OR 1.3, 95% CI 1.2-1.42) [49].

Offspring outcomes

Congenital anomalies: Pregnant women with obesity are

Supplementary Table 2: Risk of fetal structural anomalies for pregnant women with obesity.

Structural Anomaly	OR	95% CI
Neural tube defects	1.87	1.62-2.15
Spina bifida	2.24	1.86-2.69
Hydrocephaly	1.68	1.19-2.36
Cardiovascular anomalies	1.3	1.12-1.51
Septal anomalies	1.2	1.09-1.31
Cleft palate	1.23	1.03-1.47
Cleft lip and palate	1.2	1.03-1.4
Anorectal atresia	1.48	1.12-1.97
Limb reduction anomalies	1.34	1.03-1.73
Gastroschisis	0.17	0.1-0.3

Abbreviations: OR, odds ratio; CI, confidence interval.

Supplementary Table 3: Relative risk of perinatal mortality per each five-unit increase in maternal BMI.

Perinatal mortality	RR	95% CI
Fetal death	1.21	1.09-1.35
Still birth	1.24	1.18-1.3
Perinatal death	1.16	1-1.35
Neonatal death	1.15	1.07-1.23
Infant death	1.18	1.09-1.28

Fetal death: Spontaneous fetal death during pregnancy or labor; Perinatal death: Stillbirth and early neonatal death; Neonatal death: Death following a live birth but before completion of 28 days of age; Infant death: Death of a live born infant before one year of age.

Abbreviations: RR: Relative Risk.

at increased risk of having a fetus with congenital anomalies, including orofacial defects, cardiac malformations, neural tube defects (NTDs) and limb reduction abnormalities and this risk increases in proportion to the degree of maternal obesity [50] - Supplementary Table 2. The mechanism for these associations in not well understood, but it seems to be related to an altered nutritional milieu during fetal development [51]. Specifically, the increased risk of NTDs appears to be independent and unrelated to folic acid supplementation or underlying maternal diabetes [52].

By contrast, in the systematic review executed by Stothard, et al., the risk of gastroschisis was significantly reduced (OR 0.17, 95% CI .1-0.3) [50] - Supplementary Table 2.

Perinatal mortality: Even modest increases in maternal BMI carry an important risk for fetal, neonatal, and infant death [53] - Supplementary Table 3. Likewise, when compared to normal weight pregnant women, pregnant women who are overweight and with obesity have an absolute increase of 1:1000 and 2:1000 in stillbirth, respectively [54]. Potential etiologies to explain these observations include nocturnal apnea with transient oxygen desaturation and metabolic changes associated with obesity (hyperlipidemia with reduced prostacyclin production). Moreover, the risk of stillbirth enhanced with advancing gestational age among pregnant women with class 3 obesity (at 30 weeks, adjusted hazard ratio [aHR] of 1.41 versus at 37 weeks, aHR of 3.2) [55].

Large for gestational age (LGA): Both pre-pregnancy BMI and gestational weight gain play an important role in determining birth weight: When either of them rises there is an increased risk of having a LGA newborn [24,25]. Weiss, et al. proved that pregnant women with obesity have a risk twice as high of having a macrosomic newborn when compared to normal BMI women [56]. This relationship may relate to maternal and fetal hyperinsulinemia [42,57].

Childhood obesity and cardiometabolic morbidity: Fetal development in an obesogenic environment may lead to permanent changes in metabolic pathways which predisposes to an increased risk of childhood and adult diseases, such as hypertension, hyperglycemia and insulin resistance, hyperlipidemia, obesity, and coronary artery disease [58].

Neurodevelopment: Recent evidence suggests that prenatal and lactational exposure to maternal obesity are associated with psychiatric and neurodevelopment disorders in offspring, namely anxiety and depression, schizophrenia, attention deficit hyperactivity disorder, autism spectrum disorders and cognitive impairment [58,59]. Possible mechanisms for this association include dysregulated insulin, glucose, leptin, dopaminergic and serotonergic signaling, neuroinflammation and increased oxidative stress.

Asthma: Forno, et al., demonstrated an association between maternal obesity and the occurrence of asthma/wheeze in offspring (OR 1.35, 95% CI 1.08-1.68), which may be due to obesity-related changes in inflammatory pathways and dietary exposures [60].

Conclusion

It appears that pre-pregnancy BMI is a greater determinant for maternal and neonatal outcomes when compared with weight gain during pregnancy [22]. Therefore, preconception counselling is extremely important, and this period constitutes a key point in time so that women can reduce their weight and improve pregnancy and postpartum outcomes. Even a small reduction in weight is enough to have beneficial effects on pregnancy outcome and overall health [20,61].

Adipose tissue is an active endocrine organ which has deregulatory effects on vascular, metabolic, and inflammatory pathways in many organ systems and, thereby, can affect obstetric outcomes [62,63].

In the absence of medical or obstetric complications, physical activity during pregnancy is safe and must be encouraged [63,64]. Besides its benefits in decreasing the risk of GDM, hypertensive disorders, caesarean birth, and operative vaginal delivery, it can also play an essential role in the prevention of depressive conditions, especially during the postpartum period [65-70].

It is therefore imperative to encourage the adoption of healthy lifestyles, especially in the peri-conception and interpregnancy periods. Besides, there must be support in the multidisciplinary monitoring of these pregnant women to minimize associated complication rates.

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