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THE IMPACT OF INCREASED PRE-PREGNANT ADIPOSITY ON BIRTH WEIGHT INDICES

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ABSTRACT

The major and most important findings of this study support the evidence that mothers with higher BMI before pregnancy tend to give birth to heavier babies and that greater gestational weight gain has a greater effect on birth weight than pre-pregnancy BMI. Pregnant women with higher pre-pregnancy BMI and weight gain during pregnancy had newborns with higher birth weights. The greatest positive effect of gestational weight gain on birth weight occurred directly, with little mediation via cesarean delivery. There was also a positive direct effect of pre-pregnancy BMI on birth weight. However, mothers with high pre-pregnancy BMI who gained less weight during pregnancy had children with lower birth weight. These findings support the importance of improving the health care of women of reproductive age by including them in family planning programs with nutritional monitoring and education, so that they will be able to maintain an appropriate nutritional status when they plan to become pregnant and maintain an appropriate weight gain during pregnancy, with a reduced risk of complications for both mother and neonate.

KEYWORDS: Pre-Pregnant Adiposity, Birth Weight Indices.

INTRODUCTION

Obesity is a major health care concern. There is a significant association between obesity and diabetes mellitus, heart disease, stroke, and cancer. Furthermore, obesity is believed to have an influence on fertility and pregnancy outcome. In women of childbearing age, higher pre-pregnancy weight has been associated with gestational diabetes, pre-eclampsia, cesarean delivery, and infant macrosomia.[1]

In 1990, the Institute of Medicine (IOM) recommended that the body mass index (BMI) be used to define maternal weight groups. Body mass index is believed to be superior to weight-for-height as a measure of adiposity. In 1993, the American College of Obstetricians and Gynecologists (ACOG) released its BMI classification of maternal weight and optimal weight gain during pregnancy.[2] Lu et al demonstrated that the incidence of obesity at the first prenatal visit increased from 7.3% to 24.4% in the 20-year time period.

Among women aged 18–44 years in China, the prevalence of overweight/obesity increased from 19.9% to 33.5% from 1992 to 2010. On the one hand, there's a positive correlation between age and obesity rate among women of childbearing age[3], but many older women still choose to have a second child; on the other hand, some women might encounter a second pregnancy soon after the previous delivery, carrying along with some additional weight and abdominal fat mass due to high gestational weight gain and postpartum weight retention.[4]

As a consequence, the prevalence of obesity among women entering pregnancy is likely to increase, which will, in turn, result in an increase in obesity-related adverse pregnancy outcomes. Previous studies have shown that maternal pre-pregnancy overweight/obesity resulted in poor maternal and/or neonatal outcomes, such as gestational diabetes mellitus (GDM), hypertensive disorders (HID), preeclampsia, indicated preterm birth (PTB), macrosomia, large for gestational age (LGA), caesarean section (CS) and instrumental deliveries.[5]

The association between gestational weight gain (GWG) and pregnancy outcomes remains controversial. A recent study reported that women with excessive GWG had increased risks of CS and delivery of an LGA infant compared with women with adequate weight gain, but women with inadequate GWG had an increased likelihood of GDM.[6] Another study did not find any significant association between GWG and GDM. However, these studies did not control for maternal waist circumference (WC) prior to pregnancy. As an anthropometric index, the WC has been demonstrated to be more representative of visceral fat and central adiposity, and also a better predictor of obesity-related diseases such as type 2 diabetes and cardiovascular disease.[7]

Overweight/obesity in women of childbearing age is a serious public-health problem, especially in ''developing'' countries. In China, from 1992 to 2010, the prevalence of overweight or obesity in women aged 18–44 years increased from 16.8% to 26.4%, and from

3.1% to 9.0%, respectively.[8] Worryingly, these estimates of prevalence are higher in ‘‘developed’’ nations. In the UK, the prevalence of maternal obesity has more than doubled from 7.6% to 15.6% from 1989 to 2007, respectively. In women aged 20–39 years residing in North America, the prevalence of obesity increased from 13.0% to 22.0% from 1993 to 2003.[9]

In 2008, data from the Pregnancy Nutrition Surveillance System of the USA showed that the prevalence of prepregnancy obesity increased to 28.5%. The impact of pre-pregnancy body mass index (BMI) on pregnant and neonatal outcomes, as well as subsequent disease risk in the offspring, has attracted widespread attention.[10] Pre-pregnancy underweight has been shown to increase the risk of preterm birth and low birth weight (BW), as well as to increase the risk of subsequent obesity and hypertension in the offspring.[11] Prepregnancy overweight/obesity is a risk factor for diabetes mellitus (DM), hypertension, and preeclampsia in pregnancy.

However, it also increases the risk of cesarean and instrumental deliveries, hemorrhage, infection, and maternal mortality during labor. Pre-pregnancy overweight/obesity has been shown to increase the risk of the adverse neonatal outcome (e.g., preterm delivery, low/high BW, congenital anomalies, neonatal asphyxia, neonatal death, hypoglycemia, and hyperbilirubinemia), increased requirement for neonatal intensive care, and a longer duration of hospital stay.

Maternal overweight/ obesity carries an increased risk of subsequent disease risk in the offspring. This can include impaired neurodevelopmental outcome (cognitive problems, attention deficit hyperactivity disorder, and psychotic disorders), asthma, schizophrenia, insulin resistance, DM, hypertension, coronary heart disease, stroke, and even death.[12]

Description of studies

A search of three electronic databases identified 665 articles, 620 of which were excluded based on the reasons listed in Figure 1. Forty-five articles were included in the systematic review and meta-analysis: 3 case-control, in one of these studies, the impact of pre-pregnancy BMI on BW and overweight/obesity in offspring were assessed.

RESULTS

Effect of pre-pregnancy BMI on overweight/obesity in offspring Twelve reports evaluated the association between pre-pregnancy BMI and overweight/obesity in offspring. Only 4 studies[13] provided sufficient dichotomous data for prepregnancy BMI and offspring overweight/obesity and were included in the meta-analysis. Results from this analysis revealed a negative association between pre-pregnancy underweight and offspring overweight/obesity (OR, 0.46; 95% CI, 0.37–0.56; P,0.001).

In contrast, pre-pregnancy overweight or obesity was associated with an increased risk of offspring overweight/obesity in comparison with subjects with a normal BMI in the meta-analysis (OR, 1.95; 95% CI, 1.77–2.13; and OR, 3.06; 95% CI, 2.68–3.49; P,0.001). The remaining 8 studies reported the outcomes using insufficient dichotomous data and could not be pooled by the meta-analysis.

The results of these studies were non-conforming. Whitaker et al.[14] reported a retrospective cohort study in 8,494 children from low-income families who were enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children in Ohio, USA; a follow-up survey was conducted at ages 2, 3 and 4 years. That study found that pre-pregnancy underweight was associated with a decreased prevalence of childhood obesity; pre-pregnancy overweight or obesity was associated with an increased risk of childhood obesity at ages 2, 3 and 4 years.

Li et al. and Salsberry et al. analyzed the 1996 National Longitudinal Survey of Youth, Child and Young Adult data in the USA. After adjusting for potential confounders, Li et al. revealed that children at 2–14 years of age whose mothers were obese before pregnancy were also at a greater risk of becoming obese (OR, 4.1; 95% CI, 2.6–6.4; P,0.001) than children whose mothers had a normal BMI.[15]

Salsberry et al. also found the same results at follow-up of 2–3, 4–5, 6–7 years of age. The results from this analysis revealed a negative association between pre-pregnancy underweight and overweight/obesity in offspring (OR, 0.46; 95% CI, 0.37–0.56; P,0.001). In contrast to the results of the meta-analysis described above, Salsberry et al.[16] showed that pre-pregnancy underweight was not significantly associated with an increased risk of offspring obesity.

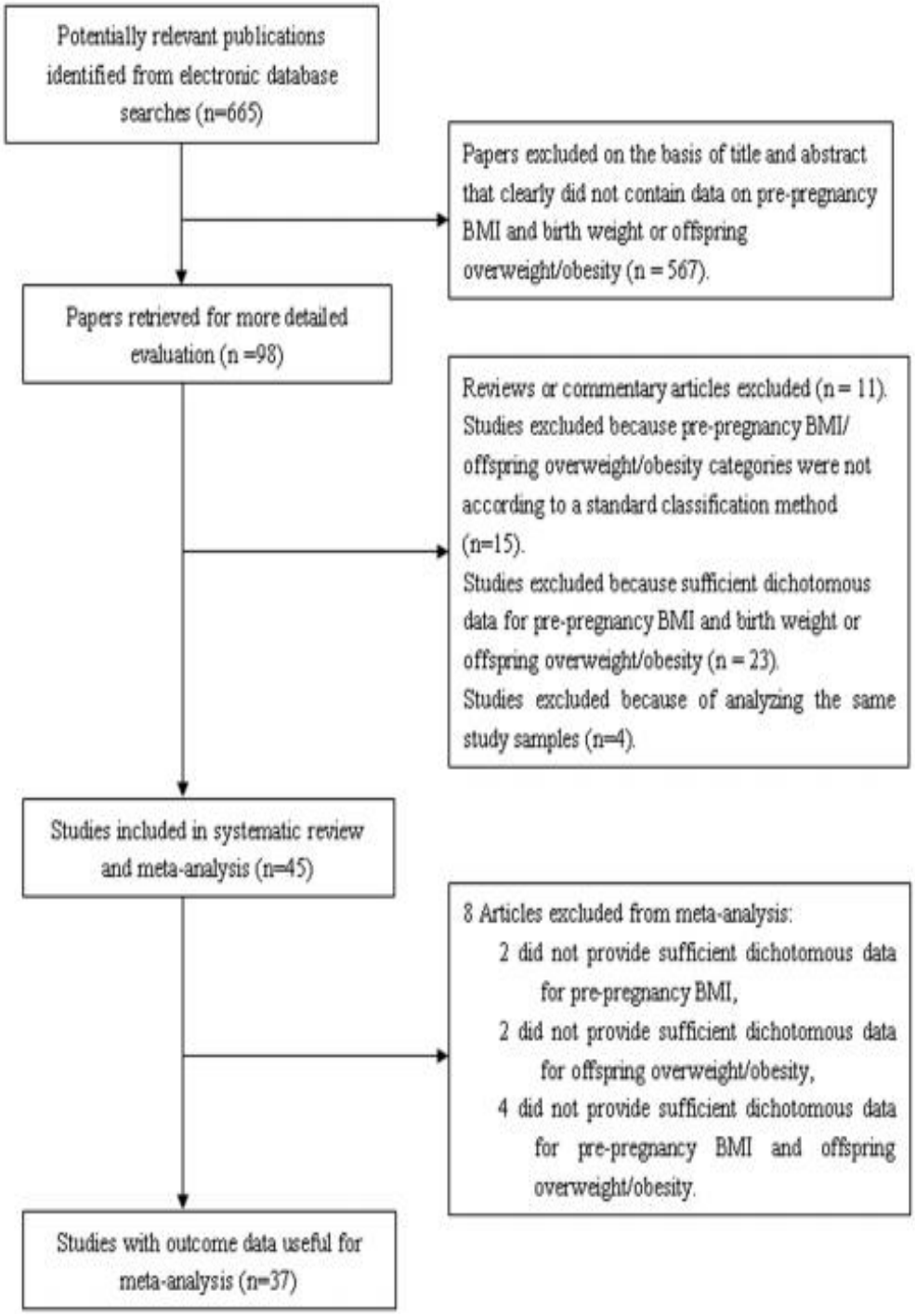

Figure 1: Screening and selection process for articles.

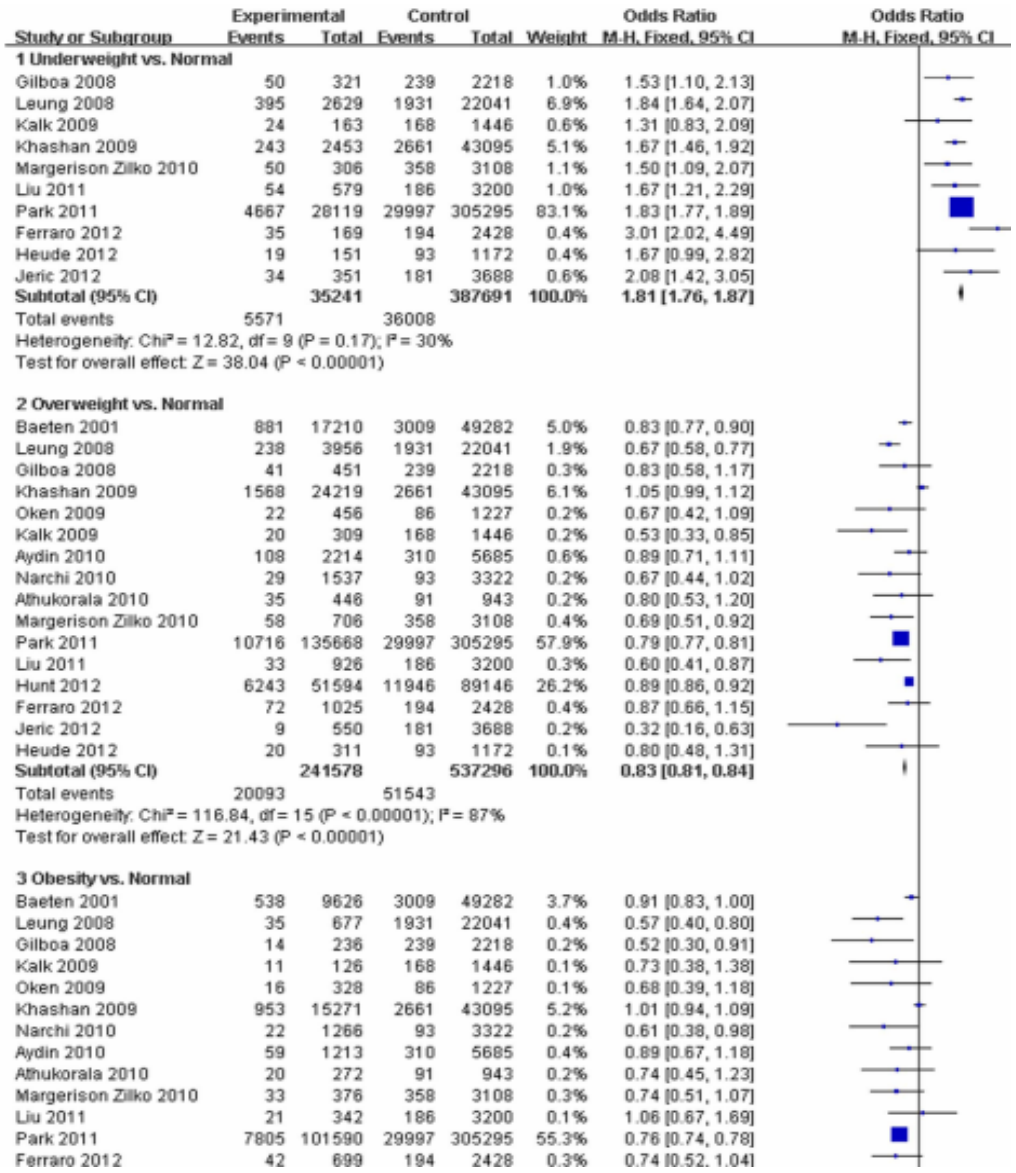

Figure 2. Forest plot of the association between pre-pregnancy BMI and being SGA.

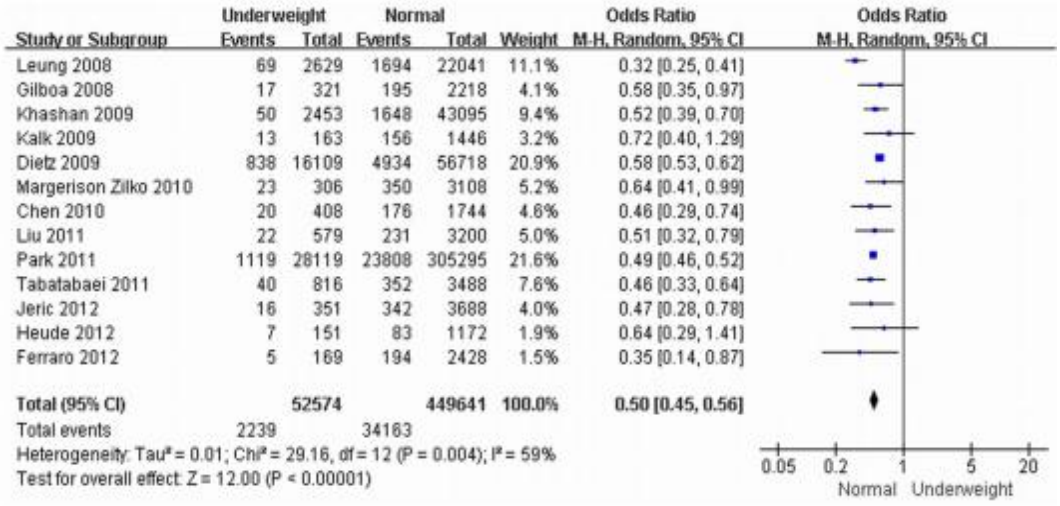

Figure 3. Forest plot of the association between pre-pregnancy underweight and being LGA.

Hawkins et al.[17] analyzed a prospective, nationally representative millennium cohort study in which 13,188 singleton children were enrolled. They showed that pre-pregnancy overweight was significantly associated with an increased risk of offspring overweight at a follow-up of 3 years of age (OR, 1.83; 95% CI, 1.66–2.02; P,0.001). Maddah et al.[18] investigated 6,635 children attending elementary schools in Rasht, Iran, by gathering data on pre-pregnancy BMI using a self-administrated questionnaire. After adjusting for potential confounders, pre-pregnancy overweight/obesity was shown to be associated with an increased risk of childhood overweight/obesity at ages 6–11 years (OR, 1.6; 95% CI, 1.1–2.3; P,0.001). Two studies chose mothers with underweight and normal weight as the control, not mothers with normal weight. Hernandez-Valero et al.[19] undertook a population-based Mexican–American cohort study and found that pre-pregnancy obesity was significantly associated with an increased risk of offspring obesity at a follow-up of 5–18 years of age (OR, 2.14; 95% CI, 1.12–4.08; P.0.001).

Janjua et al.[20] analyzed the data from a longitudinal study of pregnancy outcomes and childhood psychomotor development. They also revealed that pre-pregnancy obesity was significantly associated with an increased risk of offspring obesity at a follow-up of 5 years of age (OR, 2.92; 95% CI, 1.73–4.91; P.0.001). Analyses of heterogeneity and publication bias Heterogeneity (I 2 .50%) was high for the pooled ORs of the studies in the meta-analysis. The x 2 -test for heterogeneity was significant for the 21 studies investigating the association between pre-pregnancy obesity and LGA (x 2= 186.88, P,0.001), and this was taken into account by analyzing the data using a random model.

Sensitivity analyses were carried out, and subgroups were divided based on the differences in statistical method, study design, study method, sample size, quality grade of study, the source of pre-pregnancy BMI, pre-pregnancy BMI categories, distribution of pre-pregnancy BMI, the source of BW, and the geographic location of the study. The results showed that the differences in sample size, study method, quality grade of study, and source of pre-pregnancy BMI or infant BW made a strong impact on the association between pre-pregnancy obesity and LGA. Inspection of funnel plots did not reveal an obvious effect of publication bias, and Egger's test for publication bias was not significant (P = 0.813) for studies investigating the association between pre-pregnancy obesity and LGA.[21]

The present comprehensive systematic review and meta-analysis indicated: that pre-pregnancy underweight increased the risk of SGA and LBW; that pre-pregnancy overweight

or obesity increased the risk of LGA, HBW, macrosomia; subsequent offspring overweight/obesity in comparison with mothers with a normal BMI. The present study suggests inconsistency regarding the association between pre-pregnancy underweight and offspring overweight/obesity. Further prospective studies are needed to examine whether a causative relationship between pre-pregnancy underweight and offspring overweight/obesity exists. The systematic review provided here was developed by a robust search strategy. Furthermore, we strove to obtain information following the MOOSE recommendations. The prevalence of prepregnancy overweight/obesity is increasing in many parts of the world. Acceptance of the problem and subsequent epidemiological studies have begun in recent years, as reflected by the fact that 66.7% of the studies identified for this review were conducted between 2009 and 2012.[22]

Sources of bias in any meta-analysis are the selection and heterogeneity of the included studies. In this regard, a specific limitation of our systematic review and meta-analysis is related to the difficulty of combining studies that used different methods to assess and classify the exposure (pre-pregnancy BMI) and outcome (infant BW and offspring overweight/obesity) of the participants.

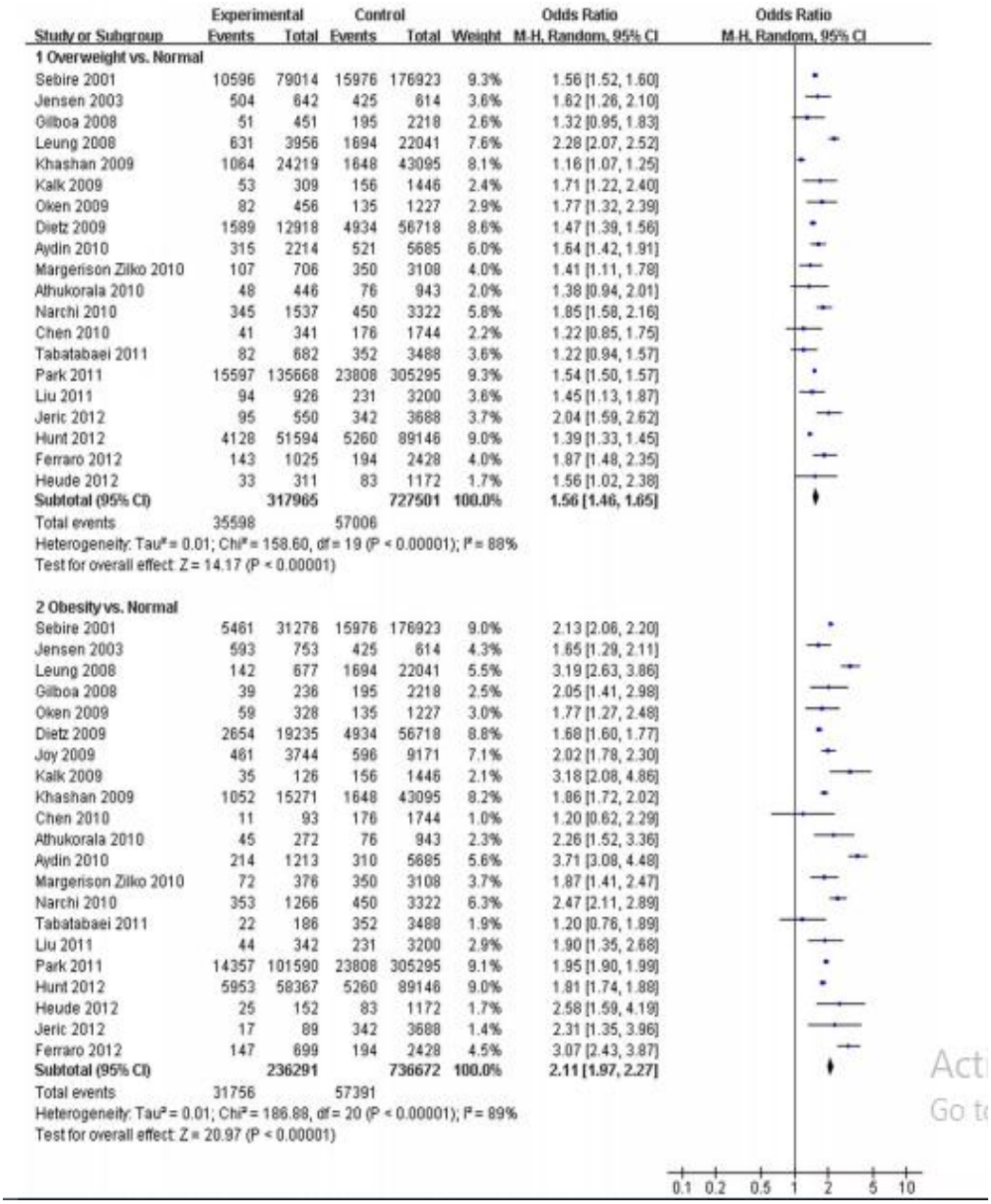

Figure 3 Forest plot of the association between pre-pregnancy overweight or obesity and being LGA.

Therefore, an adequately powered, a high-quality cohort study is needed to investigate the impact of pre-pregnancy BMI on infant BW and offspring overweight/obesity. Finally, other factors may also have contributed to the impact of pre-pregnancy BMI on BW and offspring overweight/obesity. These factors may have been maternal age, ethnicity, gestational hypertension, gestational DM, smoking during pregnancy, educational level, and gestational weight gain (GWG).[23]

Therefore, further studies should adjust for these factors and analyze them at different levels. The ‘‘fetal origins’’ hypothesis proposes that alterations in fetal nutrition results in developmental adaptations that permanently change the structure, physiology, and metabolism, thereby predisposing individuals to overweight/obesity in adulthood.[24] The process whereby a stimulus or insult at a sensitive or critical period of development has long-term effects is termed ‘‘programming’’.[25]

Malnutrition or over-nutrition in the mother has direct effects on the body size of the offspring and may contribute to the risk of overweight/obesity in later life. Some studies have found that malnutrition or over-nutrition in the mother can cause epigenetic changes in humans that persist throughout life, which might explain the conclusions of our review. The results of this review could aid better understanding of the impact of pre-pregnancy BMI on BW and offspring overweight/ obesity. They could also be useful for the regulation of prepregnancy BMI so as to reduce the risk of overweight/obesity in offspring. A systemic review encompassing 75 articles on antiobesity surgery showed that the risk of macrosomia could be lowered after maternal weight loss induced by surgery.[26]

The pre-conception of weight loss also could reduce the risk of offspring obesity at age 7 years (OR, 0.41; 95% CI, 0.20–0.83; P,0.01). For underweight mothers, adequate weight gain during pregnancy could reduce the risk of LBW and SGA. Hence, it might be possible to prevent the outcomes of offspring overweight/obesity by weight-regulation interventions in pre-pregnancy and pregnancy. According to the studies included in this review, there remain some unresolved issues. Underweight mothers have a higher risk of SGA and LBW than normal-weight mothers, and some studies have shown that infants with SGA carry an increased risk of overweight/obesity.[27]

Results from the famine in the Netherlands showed that maternal malnutrition during early gestation was associated with a higher risk of offspring overweight/obesity. Some animal studies support the association between pre-pregnancy underweight and subsequent overweight/obesity in offspring. Nevertheless, further high-quality, large-sample, mother-infant cohort studies are needed. Pre-pregnancy overweight or obesity increased the risk of LGA, HBW, macrosomia, and later offspring overweight/obesity has been confirmed in the review. Some weight-regulating intervention studies have displayed the short-term maternal and neonatal outcomes, which indicate that interventions can help pregnant and postpartum women manage their weight, decreased the risk of LGA, HBW, macrosomia. Few trials have

addressed the growth and development outcomes (offspring overweight/obesity) resulting from maternal weight loss. However, there are several ongoing randomized trials examining the impact of interventions on not only optimal maternal-fetal outcomes but also offspring obesity.[28]

In addition, BW and offspring overweight/obesity are affected by maternal age, ethnicity, gestational hypertension, and gestational DM, smoking during pregnancy, educational level, and GWG. Therefore, further studies assessing the impact of prepregnancy BMI on infant BW and offspring overweight/obesity should adjust for these factors and analyze them at different levels. Further, the impact of some important factors (GWG, smoking during pregnancy) on BW and offspring overweight/obesity need be assessed separately or interdependently with pre-pregnancy BMI. This understanding would help inform the evidence base for effective nutritional interventions in women before and during pregnancy. In conclusion, our review suggests that in comparison with mothers with a normal BMI: pre-pregnancy underweight increases the risk of SGA and LBW; pre-pregnancy overweight/obesity increases the risk of LGA, HBW, macrosomia, and subsequent offspring overweight/obesity. Recognition of this association may have important implications for primary prevention strategies for offspring overweight/obesity by targeting maternal pre-pregnancy BMI. However, this review also demonstrates other factors that may potentially mediate this association. These include maternal age, ethnicity, gestational hypertension, and gestational DM, smoking during pregnancy, educational level, and GWG. These factors must be addressed in future studies. We also offer a developmental nutrition hypothesis on potential mechanisms involving epigenetic changes induced in the embryo.[29]

We can not confirm the association between pre-pregnancy underweight and offspring overweight/obesity according to the present study: further high-quality, large-sample, mother-infant cohort studies are needed.

Birth weight is an indicator of perinatal risk and has been used in epidemiological studies as a representation of fetal nutritional exposure. A secular trend toward increased birth weight related to greater maternal weight has been observed in developed countries.[30] Birth weight reflects the conditions of pregnancy and influences the quality of life, the growth, and the development of the child, as well as childhood morbidity and mortality.[31]

Particularly important among the factors that influence birth weight are the pre-pregnancy and gestational inadequacies of the maternal nutritional status.[32] Pre-pregnancy overweight and obesity have been associated with gestational hypertension and diabetes, preterm birth, cesarean delivery, and low or high birth weight.[33] In turn, a low pre-pregnancy body mass index (BMI) has been associated with low birth weight and preterm birth.

A systematic meta-analysis of 45 studies has revealed that low pre-pregnancy BMI increases the risk of infants born small for gestational age with low birth weight, while high pre-pregnancy BMI increases the risk of infants born large for gestational age with high birth weight, macrosomia, and future overweight or obesity.[34] A systematic review of 35 studies has detected strong evidence that excessive gestational weight gain is associated with increased newborn weight (large for gestational age) and that inadequate gestational weight gain is a risk factor for lower birth weight and for small for gestational age infants.[35] An Argentinian study with 9,613 neonates using multiple (forward stepwise) linear regression models has shown that lower pre-pregnancy BMI was associated with lower birth weight, with no influence of gestational weight gain on birth weight outcome.

Despite the results showing an association of pre-pregnancy BMI and weight gain during pregnancy with birth weight, these studies have not investigated whether weight gain during pregnancy is a mediator of the association between pre-pregnancy BMI and birth weight.[36] Furthermore, most of these studies have used logistic regression analysis with simultaneous adjustment of multiple confounders.[37] This type of statistical analysis has been criticized in the literature since it only allows the investigation of associations between the explanatory variables and the outcome, without the possibility of assessing the direct and indirect effects and identifying mediating variables.[38]

CONCLUSION

We found a positive relationship between GWG and HBW, in which a higher weight gain during pregnancy predicted a higher probability of delivering HBW babies. Excessive GWG was the most significant factor associated with the delivery of HBW babies in this study. We found no significant association between pre-pregnancy BMI and HBW, but we found that the effect of GWG on birth weight was modified by pre-pregnancy BMI status. The strongest GWG–HBW association existed in the pre-pregnancy normal weight women who gained excessive weight during pregnancy.

Maternal nutrition is critical for fetal growth and development. In our study, the average GWG was 14.2 kg among normal-weight women with normal birth weight babies; our finding was lower than found in a recent publication, which indicated an average weight gain of 16.2 kg in the same BMI category of women.

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