Huai Heng Loh (Orcid ID: 0000-0002-6818-469X)

Title: The Effect of Obesity in Pregnancy and Gestational Weight Gain on Neonatal Outcome in Glucose-Tolerant Mothers

Huai Heng Loh[1], Haslinda Taipin[2], Asri Said[1]

[1] Faculty of Medicine and Health Sciences, University Malaysia of Sarawak, Malaysia

[2] Malaysia Ministry of Health Training Institute, Kota Kinabalu, Sabah, Malaysia

Keywords

Obesity; pregnancy; gestational weight gain; neonatal outcome; glucose-tolerant

Running title: Obesity in Pregnancy on Neonatal Outcome

Corresponding author

Huai Heng Loh

Faculty of Medicine and Health Sciences

University Malaysia of Sarawak

Jalan Datuk Muhammad Musa

94300 Kota Samarahan

Sarawak, Malaysia

hhloh@unimas.my

+6082-581000

Potential conflicts of interest

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/osp4.512.

None declared

Sources of funding

This study received research grant from University Malaysia Sarawak Special Grant Scheme F05/SpGS/1548/2017.

Abstract

Background

Most studies showing association between mothers with obesity in pregnancy or excessive gestational weight gain (GWG) and adverse neonatal outcome were cross-sectional or retrospective. Many included patients with gestational diabetes mellitus (GDM), which is a strong risk factor for this adverse outcome. There are no prospective studies on this topic in Malaysia. This study aimed to examine prospectively the effect of obesity in pregnancy and GWG, independent of GDM, on neonatal outcome.

Methods

Pregnant mothers in first trimester, who presented to health clinics in Kuching, were screened. Mothers with existing diabetes mellitus or GDM were excluded using 75-g OGTT during first and second trimesters. Participants with first trimester BMI≥23kg/m^2 were recruited as overweight/obese group, whereas those with BMI 18.5-22.9kg/m^2 were taken as the comparison group. At every trimester visit, mothers' weights were recorded. Babies' birth weight and occurrence of adverse neonatal outcome were documented.

Results

There were 123 mothers recruited as overweight/obese group (mean BMI 29.0kg/m^2±4.45) and 102 mothers as comparison group (mean BMI 20.4kg/m^2±1.48). The number of low birth weight was similar between groups: 9.8% in overweight/obese group, 6.9% in the comparison group (p=0.416). More than half of these babies were born to mothers with inadequate GWG (58.3% in obese group vs 57.1% in control group, p=0.077). There was no significant difference in mean birth weight (3,000g±454.5 vs 3,038g±340.8, p=0.471), preterm delivery (8.13% vs 3.92%, p=0.193) and admission rate to neonatal intensive care

unit (8.13% vs 7.85%, *p*=0.937) between groups. There was a positive correlation between total GWG in overweight/obese group on baby's weight (r=0.222, *p*=0.013). Inadequate GWG was not correlated with lower birth weight (*p*=0.052).

Conclusions

Obesity in pregnancy was not associated with poor neonatal outcome in this small sample of women in Malaysia. Total GWG showed a weak correlation with baby's birth weight in overweight/obese group.

Trial registration

Retrospectively registered with clinicaltrials.gov.my ID NCT04116268

Introduction

Obesity has long been perceived as a major risk factor in pregnancy, leading to serious short and long-term consequences for both mothers and their infants.[1] Apart from adverse pregnancy outcome, it is also associated with increased risks of adverse neonatal outcome, including preterm birth and stillbirth.[2,3] Whilst low birth weight is associated with increased risk of infant mortality,[4] macrosomia, which occurs more commonly in pregnant mothers with obesity, increases risk of obesity in the offspring at a later stage of life.[5,6] In one of a prospective analyses done in India, 46.37% of babies were macrosomic and born to mothers with pre-pregnancy obesity, whereas 19.47% macrosomia babies were born to mothers with normal pre-pregnancy weight.[7] Other studies which showed an association between mothers with obesity or having had excessive gestational weight gain and giving birth to babies with macrosomia or large for gestational age were performed as cross-sectional comparisons across births or as retrospective analyses.[8-11] Many others included mothers with co-morbidities, especially gestational diabetes mellitus (GDM), which is a well-described risk factor for adverse neonatal outcomes.[12-16] A meta-analysis of studies performed in low- or middle-income countries suggested that overweight and obesity were slightly protective against low birth weight, small for gestational age and preterm babies, but no data was presented on other adverse neonatal outcomes, such as occurrence of macrosomia and stillbirth.[17]

When pre-pregnancy body mass index (BMI) was controlled for, increased gestational weight gain contributed to a higher probability of an infant with macrosomia.[18-20] Indeed, pre-pregnancy BMI and weight gain during pregnancy are two important independent factors determining pregnancy and neonatal outcomes.[21] Gestational weight gain is stratified by BMI category and largely varies among different ethnic groups.

Data comparing neonatal outcome between mothers who have obesity and mothers with normal weight is scarce in South East Asia countries,[22,23] especially Malaysia. Although there are several published reports from Malaysia on obesity in the general population,[24,25] no prospective studies exist on effect of maternal obesity and neonatal outcome in the country. So far, the only data available is from a retrospective study which showed higher percentage of macrosomia babies among overweight and obese mothers and a positive association between gestational weight gain and neonatal outcome, ie premature birth and low birth weight.[26]

Despite these associations, obesity in pregnancy and gestational weight gain have not gained as much attention of health care providers as diabetes mellitus in pregnancy. Providers do not consider management of obesity or weight gain in pregnancy to be equally important.[27] In this observational research, the effect of obesity in pregnancy and gestational weight gain among glucose-tolerant mothers on neonatal outcome were examined prospectively, independent of diabetes mellitus, compared to normal-weight mothers. The primary objective was to examine the effect of obesity determined in first trimester of pregnancy on neonatal outcome, particularly macrosomia, whereas the secondary objective was to determine if gestational weight gain contributed to adverse neonatal outcome, compared to normal-weight mothers. It was hypothesized that obesity in pregnancy is associated with increased adverse neonatal outcomes and that gestational weight gain is positively correlated with neonatal outcomes.

Materials and Methods

Subjects

From October 2017 to April 2018, mothers in their first trimester of pregnancy who attended the maternal and child health centers in Kuching area, Sarawak, were consecutively

screened for suitability of this study. Only mothers in their first trimester of pregnancy who were more than 18 years of age and were agreeable to attend follow up at the respective clinics at least once per trimester were recruited. These mothers underwent a 75-gram oral glucose tolerance test (OGTT) on a specified date after recruitment whilst still in their first trimester. If the fasting plasma glucose was ≥7.0mmol/L, and/or 2-hour plasma glucose ≥11.1mmol/L, diagnosis of existing undiagnosed diabetes mellitus was made, and the mothers were excluded. Similarly, if the fasting plasma glucose was ≥5.1mmol/L and/or 2-hour plasma glucose was ≥8.5mmol/L, diagnosis of gestational diabetes mellitus (GDM) was made, and the mothers were also excluded from the study. These mothers then received appropriate care as per clinical practice guidelines. All the other participants were recruited and underwent follow up as per study protocol. A second 75-gram OGTT was conducted between 24-28 weeks of gestation and participants were again excluded if GDM was diagnosed. Other exclusion criteria were participants who were known to have underlying diabetes mellitus, known to have genetic disorders affecting growth or congenital anomalies upon recruitment, mothers with multiple pregnancy, those who conceived using artificial insemination, or those known to have HIV/Hepatitis B/Hepatitis C infection.

Weight gain during first trimester of pregnancy is negligible and hence the first trimester BMI is known to best reflect the pre-pregnancy BMI.[28] Participants were divided into participant group or comparison group based on the first trimester BMI.

As Asians generally have a higher percentage of body fat than Caucasians of the same age, sex, and BMI, with significantly increased risks for type 2 diabetes and cardiovascular disease even below the recommended W.H.O. BMI cut-off point of 25kg/m^2 for obesity, W.H.O. has recommended a lower BMI cut-off of 23kg/m^2 as overweight for Asians, and a BMI of ≥27.5kg/m^2 as having obesity. Based on this, participants with a BMI of ≥23kg/m^2 were recruited as obese/overweight group and those with BMI of 18.5-22.9kg/m^2 were

recruited as the comparison group. Total gestational weight gain was calculated by the difference between third trimester weight and first trimester weight.

Study protocol

Participants who fulfilled the inclusion and exclusion criteria and consented to the study were recruited. They were interviewed by the researchers in terms of their baseline demographic data. Participants' weight and height were recorded during the first visit at recruitment in their first trimester. BMI was then calculated. At every trimester visit, the mothers' weight was recorded apart from other parameters such as blood pressure and mid-stream urine for presence of proteinuria. The participants were followed up until the point of delivery. Birth weight and neonatal outcomes as outlined below were documented.

Neonatal outcomes

The outcomes measured in this study included occurrence of macrosomia and low birth weight, neonatal intensive care unit (NICU) admission, stillbirth, preterm delivery, and neonatal birth weight. Macrosomia is defined as a birth weight of 4,000g or more, whereas low birth weight is a birth weight of less than 2,500g. The term macrosomia was utilized instead of large for gestational age as evaluating a baby's weight in utero is imprecise and would only serve as a potential indication of suspected macrosomia.[29,30] Stillbirth is defined as a baby born with no signs of life at or after 28 weeks' gestation. Preterm delivery is defined as birth that occurs before the start of the 37th week of pregnancy.

Statistical analysis

Statistical analysis was performed using SPSS 19.0 (IBM Corp., Armonk, NY). Sample size calculation was based on occurrence of macrosomia, which is reported to be 19.5% among normal weight mothers and 46.4% among mothers with pre-pregnancy obesity. Using the formula by Kelsey et al for case control study,[31,32] a total sample of 100 samples

need to be recruited to give 80% power of study. Univariate analyses including chi-square was used to compare dichotomous outcomes between the groups, and Student t test was used to compare continuous outcomes. Multiple logistic regression models were used to evaluate the independent variables on the outcomes, adjusting for BMI, gestational weight gain, maternal age, parity, smoking status, and gestational age. Adjusted odds ratios and 95% confidence interval were calculated. A value of $p < 0.05$ was considered significant.

Results

Five centers were involved in this study. A total of 500 mothers in first trimester of pregnancy attending the clinic were consecutively screened. 375 subjects fulfilled the inclusion and exclusion criteria and consented to the study. A total of 120 mothers developed GDM during the later trimester and were hence excluded from the study. There were 30 mothers (18 overweight/obese and 12 with normal BMI) who did not continue with the study after recruitment due to various reasons: not willing to undergo second OGTT (n=24), transferred out to other districts (n=4), and spontaneous abortion in first trimester (n=2). There was no significant difference for maternal age, smoking status, blood pressure, BMI, education level and employment status between study participants and those who did not complete the study. A total of 123 mothers were recruited as overweight/obese group (72 were obese, 51 overweight) whereas 102 mothers were of normal BMI and were recruited as the comparison group. There was no significant difference in baseline demographic data of all subjects and are displayed in Table 1.

The mean BMI of overweight/obese group at first trimester was higher than of the comparison group (29.0kg/m^2±4.45 vs 20.4kg/m^2±1.48, p<0.001). The mean BMI of overweight mothers who were overweight during the first trimester was 25.0kg/m^2±1.29, whereas of mothers who were obese was 31.8kg/m^2±3.76. Mothers of comparison group

gained significantly more weight throughout the pregnancy compared with the overweight/obese group (total GWG of 8.4kg±3.8 vs 6.5kg±4.0, $p<0.001$). Nevertheless, 56.9% of normal-weight mothers had inadequate weight gain throughout the pregnancy as per IOM recommendations, compared to 43.1% of mothers who were overweight/obese ($p<0.001$). There was no significant difference in gestational age in between groups (overweight/obese group 267.8 days±11.0 vs comparison group 268.7 days±7.3, $p=0.953$). Mean first trimester blood pressure was significantly higher in overweight/obese group compared to the comparison group (systolic 116.4±10.1 vs 108.8±10.9, diastolic 74.4±7.9 vs 70.6±7.4, both $p<0.001$), although mean blood pressure of both groups was still within normal range.

The fetal outcomes by univariate analyses are summarized in Table 2. There were 19 babies (8.4% of total cohort) with low birth weight. 9.8% of these babies were born to mothers who were overweight/obese, compared to 6.9% in the comparison group, although the difference was not statistically significant ($p=0.416$). More than half of these babies were born to mothers with inadequate weight gain as per IOM recommendation (58.3% in overweight/obese group vs 57.1% in comparison group). Nevertheless, this difference was not statistically significant ($p=0.077$). Two babies had birth weight of >4,000g, both born to mothers from the overweight/obese group, whilst there were no macrosomia babies in the comparison group. There was no significant difference in other parameters between mothers who were overweight/obese vs normal-BMI mothers, in terms of mean birth weight (3,000g±454.5 vs 3,038g±340.8, $p=0.471$), preterm delivery (8.13% vs 3.92%, $p=0.193$) and admission rate to neonatal ICU (8.13% vs 7.85%, $p=0.937$). The indications of neonatal ICU admission are listed in Table 3. There was no stillbirth in either group.

Further analysis showed a weak but positive correlation between total gestational weight gain in overweight/obese group on baby's weight (r=0.222, $p=0.013$) but this was not

seen in the comparison group. Inadequate gestational weight gain suggests a signal towards lower birth weight; however, it was not statistically significant (p=0.052). There was no significant effect of gestational weight gain on preterm delivery (p=0.145) and admission to neonatal ICU (p=0.446) in overweight/obese group, as well as among the normal-BMI mothers (preterm delivery, p=0.679; admission to neonatal ICU, p=0.390).

Discussion

This study found that obesity in pregnancy was not associated with adverse neonatal outcome, including macrosomia, compared to mothers with normal BMI, despite having higher mean blood pressure. This contradicts previous data which showed that obesity in pregnancy is associated with higher birth weight compared to normal weight mothers, although a recent study demonstrated that pre-pregnancy obesity, in fact, might be associated with a lower probability of adverse neonatal outcome particularly pre-term birth, low birth weight and SGA.[18]

The main reason for our finding was postulated to be due to inadequate weight gain seen in this cohort of mothers, especially among women with overweight/obese and were otherwise healthy. Earlier study showed increased risk of preterm delivery and neonatal ICU admission among mothers with obesity, but was only potentiated among those with excessive gestational weight gain, those who were extremely obese, as well as those with obesity-related diseases and abruptio placentae.[33,34,35] The mean BMI of the mothers who were obese fell into the category of class I obesity. Coupled with inadequate weight gain during pregnancy, this could have contributed to a non-significant difference on adverse neonatal outcomes compared with mothers of normal BMI. Nevertheless, the relatively small sample size may have left the study under-powered to identify relationships in the present sample that have been found in other investigations.

It is interesting to note that more than 50% of the mothers who were overweight/obese had gestational weight gain below the IOM recommendations, which could explain the difference seen between our data and those reported previously. Nevertheless, the findings from this study echo what was reported by Lima et al. who also found women with higher pre-pregnancy BMI in their cohort gaining less weight during pregnancy.[36] One of the reasons of inadequate gestational weight gain among the mothers from overweight/obese group could be due to dietary restriction by managing clinicians as seen in earlier studies.[37,38]

Secondly, although the proportion of low birth weight seen in the study cohort was below of that reported in literature, this study further affirms the findings that this adverse neonatal outcome is more commonly seen among mothers with inadequate weight gain in pregnancy. Gestational weight gain below the IOM recommendations is an independent risk factor for low birth weight and is proven to lead to 2 to 2.5 times more risk for low birth weight.[39,40] Indeed, gestational weight gain seems to play a more important role in determining baby's weight compared to pre-pregnancy BMI in our population, similar to what was reported recently.[36] This association, however, was seen only among mothers who were overweight/obese in pregnancy but not in the comparison group. Nevertheless, the weak correlation suggests that birth weight may be largely pre-set by familial factors before the perinatal period.[41] In fact, the correlation between gestational weight gain and birth weight was low among women who delivered smaller children in a Japanese cohort.[41] The higher mean blood pressure among the overweight/obese group is unlikely to have contributed to this adverse neonatal outcome as the blood pressure still fell within normal range. Weight gain in low-risk pregnancies with normal pre-pregnancy BMI is less likely to contribute as a risk factor for adverse perinatal outcomes.[42] This also suggests that the focus should also be on gestational weight gain, apart from their pre-pregnancy BMI, when managing pregnancy among women who are overweight/obese.

This study has a few clinical implications. While excessive weight gain may affect maternal health leading to development of GDM and hypertension in pregnancy and increase risk of macrosomia, inadequate gestational weight gain, on the other hand, can lead to adverse neonatal outcomes particularly low birth weight, which similarly requires more attention as it is associated with increased morbidity and mortality. Hence clinicians need to strike a balance between preventing unfavorable maternal health vs adverse neonatal consequences. As pregnant mothers need to meet their own nutrition requirements on top of supplying adequate nutrients to the growing fetus,[43] more attention needs to be given, in an individualized manner, on dietary quality and nutrition of the mothers, to ensure adequate weight gain and fetal growth as minimum weight gain requirement among obese mothers may prevent small for gestational age.[39]

One limitation of this study is that it was conducted in a single district, with a small sample size, using convenient sampling method, hence the finding may not be generalized to the whole population of Malaysia at large. However, to the best of the researchers' knowledge, this is the first prospective study being done in Sarawak and Malaysia, which is a multi-racial country, examining the association between obesity in pregnancy and gestational weight gain on adverse neonatal outcome. Another limitation is lack of information on study participants' nutritional status, lifestyle and dietary pattern throughout the pregnancy, which may have affected gestational weight gain. However, by excluding underlying medical problems, such as antedated chronic hypertension, diabetes mellitus and gestational diabetes mellitus among our study participants, these confounding factors which may affect our study outcomes were avoided. GDM is a well-described risk factor for macrosomia at birth, hence, by removing this confounder, the researchers were able to study the independent effect of overweight/obesity in pregnancy. Thus, the findings from this study are able to provide valuable insights into the importance of weight management throughout pregnancy,

especially among mothers with obesity. Besides, findings from this study could put further emphasis on a more comprehensive guideline on managing obesity effectively in prenatal and antenatal care in Malaysia, as well as the importance of balanced diet in ensuring adequate gestational weight gain to reduce adverse neonatal outcome. Individual advice as to nutrient intake and adequate weight gain should be given priority among pregnant mothers, especially if they have obesity or are considered high-risk pregnancies. Both maternal weight and gestational weight gain, thus, warrant equal attention and appropriate care to reduce adverse neonatal outcome.

Another strength of this study is that by including women only from the first trimester, the researchers were able to better categorize the mothers based on their pre-pregnancy weight. Maternal memory of pre-pregnancy weight was not relied upon as this could have led to bias if the weight was not accurately recalled. BMI was utilized to categorize the study participants as it is a better indicator of body composition compared to using the weight of the mothers. The researchers also looked into the possible association between weight gain during pregnancy with neonatal outcome as obesity in pregnancy may not have been the sole factor of adverse neonatal outcome. Besides, women who developed gestational diabetes mellitus in late pregnancy were excluded through a repeated OGTT during second trimester, which could have affected study outcomes.

Conclusions

In conclusion, this study suggests that obesity in pregnancy alone does not seem to be associated with adverse neonatal outcome. If at all, it may suggest a signal towards this unfavorable consequence. On the other hand, inadequate gestational weight gain seemed to play a more pivotal role in increasing risks for adverse neonatal outcome, especially low birth weight, among mothers who are overweight/obese during pregnancy. However, the

association between these parameters cannot be concluded at this point due to the limitations of this study. Hence, more well-designed studies with larger sample sizes are crucial to examine these possible associations. Further confirmation of these findings may lead to a better change in the care and management of obesity and weight gain in pregnancy.

Declarations

Ethics approval and consent to participate

This study was conducted according to Declaration of Helsinki. The protocol was approved by the Medical Research & Ethics Committee (MREC), Ministry of Health Malaysia. This study was also registered under the National Medical Research Register (NMRR-16-2725-31652). Informed consent was obtained from all participating subjects prior to recruitment for the study. Protocol of the study was explained by recruiting doctor to each participant and consent was signed by each subject voluntarily.

Conflicts of interest

The authors declare that they have no competing interests

Acknowledgements

The authors would like to thank the Director General of Health Malaysia for the permission to publish this paper, Ms. Nadirah bt Sulaiman for statistical analysis and the Members of Obesity in Pregnancy Study Group which consists of:

Dr. Sabrina Lukas and Sr. Christina Lema from Sentosa Health Care Clinic

Dr. Lenny M. Hamden, Dr. Haslina bt Oh, Dr. Dayang Hafizah bt Awg Chee and Sr. Josie Achung from Batu Kawa Health Care Clinic

Dr. Juslina bt Omar, Dr. Isnani bt Sutiman and Sr. Monica Ak Aok from Petrajaya Health Care Clinic

Dr Jennet Michael, Sr. Habsah bt Abg Hj Busut and SN Dayang Zakariah bt Awg Aris from Tanah Puteh Health Care Clinic

Associate Professor Dr Mardiana bt Kipli, Hui Qi Chia and Sharifah Nur Azra bt Wan Hussin from Early Pregnancy Unit of Sarawak General Hospital

Professor Dr Lee Gaik Chan and Dr Janet Hii from Paediatric Unit of Sarawak General Hospital

Authors' contributions

HHL designed the conception of the study, interpreted the data, searched literature, generated figures and drafted the manuscript, HT and study group acquired the data, HT analysed the data, AS revised the manuscript. All authors had final approval of the final manuscript.

References

1. Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. Reviews in obstetrics & gynecology 2008;1:170-8.
2. Parker MG, Ouyang F, Pearson C, et al. Prepregnancy body mass index and risk of preterm birth: association heterogeneity by preterm subgroups. BMC pregnancy and childbirth 2014;14:153.
3. Amark H, Westgren M, Persson M. Prediction of stillbirth in women with overweight or obesity-A register-based cohort study. PloS one 2018;13:e0206940.
4. Altman M, Edstedt Bonamy AK, Wikstrom AK, Cnattingius S. Cause-specific infant mortality in a population-based Swedish study of term and post-term births: the contribution of gestational age and birth weight. BMJ Open 2012;2.
5. Cnattingius S, Villamor E, Lagerros YT, Wikstrom AK, Granath F. High birth weight and obesity--a vicious circle across generations. Int J Obes (Lond) 2012;36:1320-4.
6. Pham MT, Brubaker K, Pruett K, Caughey AB. Risk of childhood obesity in the toddler offspring of mothers with gestational diabetes. Obstet Gynecol 2013;121:976-82.
7. Mandal D, Manda S, Rakshi A, Dey RP, Biswas SC, Banerjee A. Maternal obesity and pregnancy outcome: a prospective analysis. J Assoc Physicians India 2011;59:486-9.
8. Ehrenberg HM, Mercer BM, Catalano PM. The influence of obesity and diabetes on the prevalence of macrosomia. Am J Obstet Gynecol 2004;191:964-8.
9. Sebire NJ, Jolly M, Harris JP, et al. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. Int J Obes Relat Metab Disord 2001;25:1175-82.
10. Baeten JM, Bukusi EA, Lambe M. Pregnancy complications and outcomes among overweight and obese nulliparous women. Am J Public Health 2001;91:436-40.
11. Hedderson MM, Weiss NS, Sacks DA, et al. Pregnancy weight gain and risk of neonatal complications: macrosomia, hypoglycemia, and hyperbilirubinemia. Obstet Gynecol 2006;108:1153-61.
12. Kumari AS. Pregnancy outcome in women with morbid obesity. Int J Gynaecol Obstet 2001;73:101-7.
13. Avci ME, Sanlikan F, Celik M, Avci A, Kocaer M, Gocmen A. Effects of maternal obesity on antenatal, perinatal and neonatal outcomes. J Matern Fetal Neonatal Med 2015;28:2080-3.
14. Toma R, Aoki S, Fujiwara K, Hirahara F. Associations of pre-pregnancy obesity with adverse pregnancy outcomes and the optimal gestational weight gain in Japanese women. Clin Exp Obstet Gynecol 2017;44:190-4.
15. Melchor I, Burgos J, Del Campo A, Aiartzaguena A, Gutierrez J, Melchor JC. Effect of maternal obesity on pregnancy outcomes in women delivering singleton babies: a historical cohort study. J Perinat Med 2019;47:625-30.
16. Hancke K, Gundelach T, Hay B, Sander S, Reister F, Weiss JM. Pre-pregnancy obesity compromises obstetric and neonatal outcomes. J Perinat Med 2015;43:141-6.
17. Rahman MM, Abe SK, Kanda M, et al. Maternal body mass index and risk of birth and maternal health outcomes in low- and middle-income countries: a systematic review and meta-analysis. Obesity reviews : an official journal of the International Association for the Study of Obesity 2015;16:758-70.
18. Averett SL, Fletcher EK. Prepregnancy Obesity and Birth Outcomes. Matern Child Health J 2016;20:655-64.
19. Ludwig DS, Currie J. The association between pregnancy weight gain and birthweight: a within-family comparison. Lancet 2010;376:984-90.
20. Lawlor DA, Lichtenstein P, Fraser A, Langstrom N. Does maternal weight gain in pregnancy have long-term effects on offspring adiposity? A sibling study in a prospective cohort of 146,894 men from 136,050 families. Am J Clin Nutr 2011;94:142-8.
21. Choi SK, Park IY, Shin JC. The effects of pre-pregnancy body mass index and gestational weight gain on perinatal outcomes in Korean women: a retrospective cohort study. Reprod Biol Endocrinol 2011;9:6.

22. Soltani H, Lipoeto NI, Fair FJ, Kilner K, Yusrawati Y. Pre-pregnancy body mass index and gestational weight gain and their effects on pregnancy and birth outcomes: a cohort study in West Sumatra, Indonesia. BMC Womens Health 2017;17:102.
23. Sunsaneevithayakul P, Titapant V, Ruangvutilert P, et al. Relation between gestational weight gain and pregnancy outcomes. J Obstet Gynaecol Res 2014;40:995-1001.
24. Lim KG. A Review of Adult Obesity Research in Malaysia. Med J Malaysia 2016;71:1-19.
25. Mohamad Nor NS, Ambak R, Mohd Zaki N, et al. An update on obesity research pattern among adults in Malaysia: a scoping review. BMC Womens Health 2018;18:114.
26. Rozlan N, Majid HAMA, Abas SS, Danis A, Isa KAM. The Association of Gestational Weight Gain and the Effect on Pregnancy Outcome Defined by BMI Group among Women Delivered in Hospital Kuala Lumpur (HKL), Malaysia: A Retrospective Study. Asian Journal of Clinical Nutrition 2012;4:160-7.
27. Chang T, Llanes M, Gold KJ, Fetters MD. Perspectives about and approaches to weight gain in pregnancy: a qualitative study of physicians and nurse midwives. BMC pregnancy and childbirth 2013;13:47.
28. Usha Kiran TS, Hemmadi S, Bethel J, Evans J. Outcome of pregnancy in a woman with an increased body mass index. BJOG : an international journal of obstetrics and gynaecology 2005;112:768-72.
29. Kc K, Shakya S, Zhang H. Gestational Diabetes Mellitus and Macrosomia: A Literature Review. Annals of Nutrition and Metabolism 2015;66(suppl 2):14-20.
30. Ray EM, Alhusen JL. The Suspected Macrosomic Fetus at Term: A Clinical Dilemma. J Midwifery Womens Health 2016;61:263-9.
31. Kelsey JL WA, Evans AS, Thompson WD. Methods in Observational Epidemiology: Oxford Unviversity Press; 1996.
32. JL F. John Wiley & Sons; 1981.
33. Nohr EA, Bech BH, Vaeth M, Rasmussen KM, Henriksen TB, Olsen J. Obesity, gestational weight gain and preterm birth: a study within the Danish National Birth Cohort. Paediatr Perinat Epidemiol 2007;21:5-14.
34. Flick AA, Brookfield KF, de la Torre L, Tudela CM, Duthely L, Gonzalez-Quintero VH. Excessive weight gain among obese women and pregnancy outcomes. Am J Perinatol 2010;27:333-8.
35. Crane JM, Murphy P, Burrage L, Hutchens D. Maternal and perinatal outcomes of extreme obesity in pregnancy. J Obstet Gynaecol Can 2013;35:606-11.
36. Lima R, Batista RFL, Ribeiro MRC, et al. Prepregnancy body mass index, gestational weight gain, and birth weight in the BRISA cohort. Revista de saude publica 2018;52:46.
37. Eastman NJ, Jackson E. Weight relationships in pregnancy. I. The bearing of maternal weight gain and pre-pregnancy weight on birth weight in full term pregnancies. Obstetrical & gynecological survey 1968;23:1003-25.
38. Simpson JW, Lawless RW, Mitchell AC. Responsibility of the obstetrician to the fetus. II. Influence of prepregnancy weight and pregnancy weight gain on birthweight. Obstetrics and gynecology 1975;45:481-7.
39. Hannaford KE, Tuuli MG, Odibo L, Macones GA, Odibo AO. Gestational Weight Gain: Association with Adverse Pregnancy Outcomes. Am J Perinatol 2017;34:147-54.
40. Li C, Liu Y, Zhang W. Joint and Independent Associations of Gestational Weight Gain and Pre-Pregnancy Body Mass Index with Outcomes of Pregnancy in Chinese Women: A Retrospective Cohort Study. PLoS One 2015;10:e0136850.
41. Sato N, Miyasaka N. Stratified analysis of the correlation between gestational weight gain and birth weight for gestational age: a retrospective single-center cohort study in Japan. BMC Pregnancy Childbirth 2019;19:402.
42. Eraslan Sahin M, Col Madendag I. Effect of Gestational Weight Gain on Perinatal Outcomes in Low Risk Pregnancies with Normal Prepregnancy Body Mass Index. BioMed Research International 2019;2019:3768601.
43. Ramachandran P. Maternal nutrition--effect on fetal growth and outcome of pregnancy. Nutrition reviews 2002;60:S26-34.

Table 1 Baseline demographic data of pregnant subjects

	Overweight/Obese (n=123)	Comparison (n=102)	*p*
Age, mean (SD)	30.1 (5.0)	28.9 (4.9)	0.09
Education level, n (%)			0.71
No formal education	1 (0.81)	1 (0.98)	
Primary	5 (4.07)	5 (4.90)	
Secondary	73 (59.35)	67 (65.69)	
Tertiary	44 (35.77)	29 (28.43)	
Employment status, n (%)			0.42
Employed	66 (53.0)	61 (59.0)	
Unemployed	57 (47.0)	41 (41.0)	
Household income, median (IQR)	24,000 (30,000)	24,000 (21,900)	0.37
Smoking status, n (%)			1.0
Yes	1 (0.81)	1 (0.98)	
No	122 (99.2)	101 (99.0)	
Family history of Type 2 Diabetes, n (%)			0.12
Yes	27 (22.0)	14 (13.7)	
No	96 (78.1)	88 (86.3)	
Family history of Hypertension, n (%)			0.07
Yes	52 (42.3)	31 (30.4)	
No	71 (57.7)	71(69.6)	
Family history of Cardiovascular disease, n (%)			0.18
Yes	11 (8.9)	4 (3.9)	
No	112 (91.1)	98 (96.1)	
Body mass index, kg/m^2	29.0 (4.45)	20.4 (1.48)	<0.001
Gestational age, days	267.8±11.0	268.7±7.3	0.953
Gestational weight gain, kg	6.5kg±4.0	8.4kg±3.8	<0.001
Systolic blood pressure, mmHg	116.4±10.1	108.8±10.9	<0.001
Diastolic blood pressure, mmHg	74.4±7.9	70.6±7.4	<0.001

Table 2 Univariate analysis on neonatal outcome in between groups

	Overweight/Obese (n=123)	Comparison (n=102)	p
Mean birth weight, g (SD)	3,000 (454.5)	3,038 (340.8)	0.471
Low birth weight, n (%)	12 (9.8)	7 (6.9)	0.416
Macrosomia, n (%)	2 (1.6)	0 (0)	NA
Preterm delivery, n (%)	10 (8.1)	4 (3.9)	0.193
NICU admission, n (%)	10 (8.1)	8 (7.9)	0.937
Stillbirth, n (%)	0 (0)	0 (0)	NA

Table 3 Reasons for Neonatal Intensive Care Unit (NICU) admission

Reasons for NICU admission	Overweight/Obese n (%)	Comparison n (%)
Premature birth	6 (4.9)	2 (2.0)
Presumed sepsis	2 (1.6)	4 (3.9)
G6PD deficiency	1 (0.8)	1 (1.0)
Moderate hypoxic ischemic encephalopathy	1 (0.8)	1 (1.0)
Total	**10 (8.1)**	**8 (7.8)**