**Mini-CAT**

Clinical Question: 28-year-old female patient with a BMI of 35 who is otherwise healthy wants to know if she has a higher chance of having a miscarriage than women who are of average weight.

PICO Question:

In females of childbearing age, does obesity affect the risk for miscarriage in pregnancy?

**P-**Women of childbearing age

**I-**Obesity

**C-** average weight

**O-**miscarriage

|  |  |  |  |
| --- | --- | --- | --- |
| **P** | **I** | **C** | **O** |
| Female | Obesity | Women of average weight | Miscarriage |
| Maternal | Increased BMI |  | Spontaneous abortion |
| Childbearing women |  |  | Pregnancy loss |

Search Strategy:

Searched Terms: “Maternal obesity miscarriage”

Database and Articles Returned:

Cochrane: Maternal obesity → 161 reviews

Pubmed: Maternal obesity miscarriage → 194

Pubmed: Increase BMI risk for miscarriage → 229

Google Scholar: Maternal obesity miscarriage→ → 12,000

Filters: Humans; female; Best match; free; full article; English, since 2016

Selection Methods:

* Systematic reviews, meta analyses, cohort studies, prospective cohort and retrospective cohort studies
* Appropriateness to the research question, maternal obesity (and not paternal) only
* Studies focusing on the risk for miscarriage and not other birth complications
* Age of study subjects, ie of childbearing age
* While there were many articles written on the subject, majority of them were from over five years ago so it was difficult to obtain a relevant article that was recent and of the highest level of evidence.

Articles Chosen for Inclusion (please copy and paste the abstract with link):

Article #1:

Article type: Meta-Analysis

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5954173/>

Stubert, J., Reister, F., Hartmann, S., & Janni, W. (2018). The risks associated with obesity in pregnancy. *Deutsches Ärzteblatt International*, *115*(16), 276.

Summary

Background: Approximately one-third of all women of childbearing age are overweight or obese. For these women, pregnancy is associated with increased risks for both mother and child.

Methods: This review is based on pertinent publications retrieved by a selective search of PubMed, with special attention to current population-based cohort studies, systematic reviews, meta-analyses, and controlled trials.

Results: Obesity in pregnancy is associated with unfavorable clinical outcomes for both mother and child. Many of the risks have been found to depend linearly on the body-mass index (BMI). The probability of conception declines linearly, starting from a BMI of 29 kg/m2 , by 4% for each additional 1 kg/m2 of BMI (hazard ratio 0.96, 95% confidence interval: [0.91; 0.99]). A 10% increase of pregravid BMI increases the relative risk of gestational diabetes and that of preeclampsia by approximately 10% each. A 5 kg/m2 increase of BMI elevates the relative risk of intrauterine death to 1.24 [1.18; 1.30]. An estimated 11% of all neonatal deaths can be attributed to the consequences of maternal overweight and obesity. Nonetheless, in most randomized controlled trials, nutritional and lifestyle interventions did not bring about any clinically relevant reduction in the incidence of gestational diabetes and fetal macrosomia.

Conclusion: The risks associated with obesity in pregnancy cannot necessarily be influenced by intervention. Preventive measures aimed at normalizing body weight before a woman becomes pregnant are, therefore, all the more important.

Article #2

Article type: Prospective Cohort

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4720950/>

Al-Hakmani, Fatma M., et al. "The effect of obesity on pregnancy and its outcome in the population of Oman, Seeb Province." *Oman medical journal* 31.1 (2016): 12.

Abstract

Objectives

The World Health Organization estimated that in 2011 worldwide 1.6 billion adults were overweight, and 400 million were obese. The obesity epidemic is a documented phenomenon and Oman is no exception. The aim of this study was to determine the effect of obesity on pregnancy and its prenatal and neonatal outcomes.

Methods

A prospective cohort study was carried out among pregnant Omani women attending antenatal clinics in their first trimester in the Seeb province of Muscat, Oman.

Results

A total of 700 pregnant women were enrolled in the study and were categorized according to their body mass index: 245 (35%) were normal weight, 217 (31%) were overweight, and 238 (34%) were obese. The relative risk (RR) of cesarean section among obese women compared to women of normal weight was 2.1 (95% confidence interval (CI) 1.2–3.2) and of overweight women was 1.4 (95% CI 0.9–2.3). The risk of elective cesarean section increased to 7.5 (95% CI 1.7–32.8) in obese women and was statistically significant in the obese group. In this study, 100 women (15.7%) developed gestational diabetes (11.8% of normal weight women, 17.8% of overweight women, and 17.9% of obese women). Miscarriages were more common among obese women 11.9% (n = 27) compared to the normal weight and overweight groups (6.7% and 9.4%, respectively). There was a weak yet statistically significant correlation between birth weight and body mass index. The risk of macrosomia was significantly higher in obese women compared to normal weight women. To evaluate the sensitivity of the oral glucose challenge test (OGCT), the oral glucose tolerance test (OGTT) was measured in 203 participants (29%) who had a normal OGCT result. It was found that 14.5% of overweight women and 13.5% of normal weight women had an abnormal OGTT result even when their OGCT result was normal.

Conclusions

Obesity is associated with an increased risk of cesarean section (especially elective cesarean), gestational hypertension, macrosomia, and miscarriage. It also increases the risk of gestational diabetes.

Article #3

Article Type: Prospective Cohort

<https://www.ncbi.nlm.nih.gov/pubmed/31070002>

Zhou, Yubo, et al. "Association of Maternal Obesity in Early Pregnancy with Adverse Pregnancy Outcomes: A Chinese Prospective Cohort Analysis." *Obesity* 27.6 (2019): 1030-1036.

Abstract

Objective

This study aimed to examine the associations of maternal obesity in early pregnancy with adverse pregnancy outcomes.

Methods

A prospective cohort analysis was performed among 18,481 Chinese nulliparous women, using data from a 2006 to 2009 trial of prenatal micronutrient supplementation. Obesity was defined as BMI ≥ 27.5 kg/m2. Interested outcomes included fetal loss (spontaneous abortion plus stillbirth), infant death, total mortality, and preterm and birth weight outcomes.

Results

Compared with normal weight, obesity was associated with total mortality (adjusted relative risks [ARR] 1.34; 95% CI: 1.03‐1.74) and fetal loss (ARR 1.51; 95% CI: 1.15‐1.99) but not with infant death (ARR 0.53; 95% CI: 0.20‐1.46). Further analyses showed that obesity was particularly associated with spontaneous abortion (ARR 1.51; 95% CI: 1.13‐2.02) rather than stillbirth (ARR 1.52; 95% CI: 0.65‐3.57). Moreover, obesity was associated with preterm birth (ARR 1.59; 95% CI: 1.25‐2.02), macrosomia (ARR 3.71, 95% CI: 3.01‐4.59), and large for gestational age (ARR 2.93; 95% CI: 2.49‐3.47).

Conclusions

Maternal obesity in early pregnancy is associated with various adverse pregnancy outcomes in Chinese nulliparous women, suggesting the importance of an appropriate weight before and during pregnancy.

Article #4

Article Type: Retrospective Cohort

<https://www.ncbi.nlm.nih.gov/pubmed/27789185>

Tremellen, Kelton, Karma Pearce, and Deidre Zander-Fox. "Increased miscarriage of euploid pregnancies in obese women undergoing cryopreserved embryo transfer." *Reproductive biomedicine online* 34.1 (2017): 90-97.

Abstract

Obesity is known to be associated with an increased risk of miscarriage after natural and assisted conception. Although most sporadic miscarriages are caused by genetic abnormalities, it is presently uncertain if genetics is also the underlying mechanism leading to increased pregnancy loss seen in obese women. Karyotyping of the products of conception suggests a reduced rate of fetal aneuploidy in miscarriages from obese compared with lean individuals. Karyotype analysis, however, is prone to false negative results because of inadvertent culture of maternal rather than fetal tissue. Therefore, to better analyze the effect of the genetic status on obesity-related miscarriage, we retrospectively analyzed the outcomes 125 consecutive cryopreserved embryo transfer cycles resulting in a pregnancy after screening for genetic normality using comparative genomic hydridization. Lean individuals (body mass index 18.5-24.9 kg/m2) had a significantly lower rate of miscarriages (14.2%) than overweight (29.1%) or obese (41.9%) women (P = 0.001); this relationship remained significant (P = 0.023) even after adjusting for relevant confounders, e.g. maternal age, cause of infertility, number of previous IVF cycles, type of frozen embryo transfer cycle or past obstetric history. These results support a non-genetic cause for obesity-related miscarriage.

Article #5

Article Type: Retrospective Cohort

<https://www.ncbi.nlm.nih.gov/pubmed/26523329>

Provost, Meredith P., et al. "Pregnancy outcomes decline with increasing recipient body mass index: an analysis of 22,317 fresh donor/recipient cycles from the 2008–2010 Society for Assisted Reproductive Technology Clinic Outcome Reporting System registry." *Fertility and sterility* 105.2 (2016): 364-368.

Abstract

OBJECTIVE:

To examine the effect of recipient body mass index (BMI) on IVF outcomes in fresh donor oocyte cycles.

DESIGN:

Retrospective cohort study.

SETTING:

Not applicable.

PATIENT(S):

A total of 22,317 donor oocyte cycles from the 2008-2010 Society for Assisted Reproductive Technology Clinic Outcome Reporting System registry were stratified into cohorts based on World Health Organization BMI guidelines. Cycles reporting normal recipient BMI (18.5-24.9) were used as the reference group.

INTERVENTION(S):

None.

MAIN OUTCOME MEASURE(S):

Implantation rate, clinical pregnancy rate (PR), pregnancy loss rate, live birth rate.

RESULT(S):

Success rates and adjusted odds ratios with 95% confidence intervals for all pregnancy outcomes were most favorable in cohorts of recipients with low and normal BMI, but progressively worsened as BMI increased.

CONCLUSION(S):

Success rates in recipient cycles are highest in those with low and normal BMI. Furthermore, there is a progressive and statistically significant worsening of outcomes in groups with higher BMI with respect to clinical pregnancy and live birth rate.

**Summary of the Evidence**:

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| --- | --- | --- | --- | --- | --- |
| Author (Date) | Level of Evidence | Sample/Setting  (# of subjects/ studies, cohort definition etc. ) | Outcome(s) studied | Key Findings | Limitations and Biases |
| Stubert, J., Reister, F., Hartmann, S., & Janni, W. (2018). The risks associated with obesity in pregnancy. *Deutsches Ärzteblatt International*, *115*(16), 276. | Level 1, meta-analysis and systematic review | A pooled analysis of six studies comparing obese (n = 3800) with normal-weight women (n = 17 146).  Population-based cohort studies, randomized controlled trials, systematic reviews, and meta-analyses  were preferentially included in the analysis. | Miscarriage rate after spontaneous conception; recurrent miscarriage; euploid miscarriages | - 13.6% versus 10.7% miscarriage rate in obese versus normal-weight women.  - 0.4% versus 0.1% recurrent miscarriage rate  - 58% [18/31] versus 37% [32/86] increased risk for euploid miscarriages  - Overweight and obesity during pregnancy result in increased  maternal and fetal morbidity in relation to BMI. | Having more studies included in the meta-analysis could have bolstered the evidence further.  -Including data on paternal BMI could have been another significant parameter to study. |
| Al-Hakmani, Fatma M., et al. "The effect of obesity on pregnancy and its outcome in the population of Oman, Seeb Province." *Oman medical journal* 31.1 (2016): 12. | Level 3  Prospective cohort | 700 pregnant women in their first trimester were enrolled in the study from across all primary health care centers in the Seeb province of Muscat, Oman, between March 2011 and April 2012. 245 (35%) normal weight, 217 (31%) overweight, 238 (34%) obese.  The mean age of women was 29.0±5.6 years | Risk for cesarean sections, gestational hypertension, miscarriage | -Obese women were more likely to have a cesarean section or induced delivery  -None of the women in the normal weight group developed gestational hypertension compared to 5.7% of the obese women did.  -Obese women had higher percentage of miscarriages compared to normal weight women: 11.9% compared to 6.7%  - Even with adequate prenatal care, obesity is associated with increased adverse effects on pregnancy and its outcome. | The study was limited to one geographical area of Muscat Governorate which has a large, urbanized population. The results would be more generalizable if they included other areas in Oman with more diverse population. |
| Zhou, Yubo, et al. "Association of Maternal Obesity in Early Pregnancy with Adverse Pregnancy Outcomes: A Chinese Prospective Cohort Analysis." *Obesity* 27.6 (2019): 1030-1036. | Level 3  Prospective Cohort | Data from a 2006-2009 RCT (of prenatal micronutrient supplements) was used. 18,481 nulliparous women in their first trimester in five counties in Hebei Province of China were included in this study. Obesity was defined as BMI ≥ 27.5 kg/m2. 1,086 women were underweight, 11,096 women were normal weight, 5,377 were overweight and 922 were obese. | Various offspring mortality indicators including spontaneous abortion, stillbirth, fetal loss, neonatal death, infant death and total mortality and other adverse pregnancy outcomes such as low birth weight and preterm birth. | -Compared to normal weight women, overweight and obesity had increased risk of fetal loss (overweight: adjusted RR, 1.21, 95% CI: 1.03‐1.42; obesity: adjusted RR, 1.51, 95% CI: 1.15‐1.99) and particularly with spontaneous abortion (overweight: adjusted RR, 1.25, 95% CI: 1.06‐1.48; obesity: adjusted RR, 1.51, 95% CI: 1.13‐2.02) Also with higher risk of preterm delivery. | This study used results from a different control trial. While the researchers were confident that the data they were using was correct, there is always a risk for inaccuracies when relying on data from others and not conducting the research oneself. Also, although the sample size is large the ratio of obese to normal weighted women is far from even which may skew the results.  This research also defined obesity with a lower threshold than is used in other countries. |
| Tremellen, Kelton, Karma Pearce, and Deidre Zander-Fox. "Increased miscarriage of euploid pregnancies in obese women undergoing cryopreserved embryo transfer." *Reproductive biomedicine online* 34.1 (2017): 90-97. | Level 3  Retrospective Analysis | Patients undergoing PGS treatment (aneuploidy screening) at a private infertility clinic between November 2012 and December 2014. All participants underwent subsequent cryopreserved transfer of a euploid embryo. Of the 125 women, 70 were lean, 24 were overweight and 31 were obese (BMI >30) | Pregnancies that failed by the eight week ultrasound, overall miscarriage rate, and rate of miscarriage in women on artificial hormone replacement cycles (rather than ovular cycles) in women undergoing cryopreserved embryo transfer. | - The proportion of pregnancies that failed by the 8-week ultrasound increased from 14.2% in the lean group, 29.1% in the overweight group and 41.9% in the obese groups.  - overall rate of miscarriage in the overweight and obese group was significantly higher than seen in the lean group (36.4% versus 14.3%; P = 0.006).  - the rate of miscarriage in the entire cohort was also significantly higher in women on artificial hormone replacement cycles than ovular cycles (45% versus 17%; P = 0.003), with this difference being even more marked in the overweight and obese sub-group (61.1% versus 24.3%; P = 0.015). | -The sample size is very small, with only 31 obese patients enrolled.  -Because all these patients were undergoing PGS (which is not standard practice yet at that IVF clinic) the cohort used is likely to be older and have had more fertility treatments than the average IVF patient. |
| Provost, Meredith P., et al. "Pregnancy outcomes decline with increasing recipient body mass index: an analysis of 22,317 fresh donor/recipient cycles from the 2008–2010 Society for Assisted Reproductive Technology Clinic Outcome Reporting System registry." *Fertility and sterility* 105.2 (2016): 364-368. | Level 3  Retrospective Cohort | 22,317 donor/recipient IVF cycles using data from the  Society for Assisted Reproductive Technology Clinic Outcome  Reporting System (SART CORS) database from 2008 to 2010.  SART CORS (or SART) is a self-reported database in the United  States that represents approximately 97% of the clinical activity of US IVF clinics. | Clinical pregnancy, pregnancy loss (defined as pregnancy ending before 24 completed weeks of gestation), live birth rate (delivery of live-born infant at >24 weeks gestation.) | -There was a trend towards lower implantation rates with increasing BMI  - The rate of pregnancy loss increased steadily from  8.6% in the reference group to 15.9% in patients with a BMI  of 40–44.9.  - For obese patients with BMI between 30 and 34.9, the clinical PR decreased 6% from the reference value (OR 0.77, 95% CI 0.69–0.87; P<.001 | The study was not able to include male partner/donor BMI which has been shown to correlate with pregnancy outcomes in IVF in some studies.  -With such a large study population there is the possibility for input errors that reduces the accuracy of the data.  -The study was not able to control for racial differences  -Only small percentage of the 22,317 cycles included in the study only 1,212 occurred women with BMI >35. This may have affected the data and caused some of the results from the higher BMI categories to not achieve statistical significance. |

Conclusion(s):

Maternal obesity is a significant risk factor for miscarriage in pregnancy. Although the mechanism of action for this outcome is not agreed upon by all by all the studies included in my research, there was a significant trend towards adverse pregnancy outcomes and increased BMI. There was some discrepancy between the studies used because each of them defined the parameters of average weight, overweight, obesity, and levels of obesity using slightly different BMI intervals, but despite this the statistical significance of their conclusions are still strong. The studies included were also from many different countries, including Oman, China, United States, and Australia which bolsters the generalizability of the results to apply to women around the world. Many of the studies recommended that more research be done on the topic, including keeping record of paternal (or in the case of IVF, the donor) BMI to see if there is a link between that and miscarriage or poor pregnancy outcomes. Some articles also included recommendations to OBGYN or IVF clinics to help the women lose weight before they get pregnant rather than the patient attempting to lose weight once already pregnant. More studies need to be done to determine whether increasing or lowering BMI during pregnancy influences the rate of miscarriages.

Clinical Bottom Line:

Please include an assessment of the worth to practice

According to the most recent evidence-based medicine, my conclusion for the obese patient is that obesity does increase the risk for miscarriage in pregnancy.