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Posted Date: 2 August 2024

doi: 10.20944/preprints202408.0119.v1

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Article

Fetal Growth Following Electronic Cigarette Use in Pregnancy

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Abstract: Electronic cigarette (ecig) use in pregnancy is common, but potential effects on fetal development are largely unknown. The study goal was to examine the association between ecig exposure and fetal growth. Data were extracted from medical charts in this single site retrospective study. The sample, excluding those with known tobacco, alcohol, illicit drug, opioid, and benzodiazepine use, contained women who used ecigs throughout pregnancy and non-ecig user controls. Fetal size measurements from second and third trimester ultrasounds and at birth were expressed as percentiles for gestational age. Following adjustment for confounding factors, in the second trimester, only femur length was significant, with an adjusted deficit of 11.5 percentile points for ecig exposed compared to controls. By the third trimester, femur length difference was 28.5 points, with fetal weight difference also significant (17.2 points). At birth, all three size parameter differences between groups were significant. Significant size deficits were predicted by prenatal ecig exposure, becoming larger and impacting more parameters with increasing gestation. While additional study is warranted to confirm and expand upon these findings, this study adds to emerging data pointing to specific harms following ecig exposure in pregnancy, and suggests that ecigs may not be a “safer” alternative to combustible cigarette smoking in pregnancy.

Keywords: Electronic cigarettes; Pregnancy smoking; Fetal growth; Birth size

1. Introduction

Combustible cigarette (CC) use in pregnancy is the current leading cause of poor pregnancy outcomes [1]. Published human studies demonstrate immediate harms due to CC use in pregnancy including fetal growth restriction, low birth weight (LBW), small for gestational age (SGA), preterm birth (PTB), pulmonary hypoplasia, increased rates of cesarean delivery, birth defects, admission to the neonatal intensive care unit, and fetal or neonatal death [2–5]. The use of electronic nicotine delivery systems, including electronic cigarettes (ecig), in pregnancy and their associated fetal and neonatal outcomes are less understood, but growing evidence suggests they are not insignificant and warrant further investigation. The American College of Obstetricians and Gynecologists (ACOG) recommends cessation of smoking in all forms during pregnancy [6], though studies have indicated the general public believes ecigs to be safer alternatives in pregnancy [7].

Recent increased use and popularity of ecigs has furthered the discussion of specific harms of cigarettes in pregnancy, as up to 15% of pregnancies in the U.S. involve ecig use [8]. Animal studies using zebrafish models have shown associations between exposure to ecig aerosols and impaired bone and cartilage development [9]. Further, cinnamaldehyde flavoring in nicotine-free EC was associated with decreased cleithrum and bone length in zebrafish embryos [9]. In relation to prenatal exposure to ecig vapor in mouse models, some studies demonstrated a significant reduction in birthweight [10,11], as well as decreased adult weight [12,13]. Human studies have found ecig use in pregnancy to be linked to increased risk for babies being born SGA [14–16], LBW [15,17–19], and preterm [15,17,18].

There are presently no published human studies that examine the specific growth parameters affected by use of ecigs. However, fetal growth deficits following CC use in pregnancy have been examined across several studies. Literature supports that effects are largely influenced by trimester of pregnancy corresponding with CC use. There are inconsistent findings across studies about whether CC use in the second trimester of pregnancy predicts decreased head circumference (HC), biparietal diameter (BPD), abdominal circumference (AC), mean abdominal diameter (MAD), or estimated fetal weight (EFW) [2,20–30]. Femur length (FL), however, was consistently found to be significantly reduced in the second trimester following maternal CC use [2,26,28]. When assessing fetal growth parameters in the third trimester, many of these same studies found decreased AC, MAD, and EFW in association with maternal CC use [20–22,25,26,29–34]. When examining FL in the third trimester, studies found either decreased FL [21,23,25,26,29,30] or no significant impact on FL [20,22,34,35] relative to maternal CC use in pregnancy. There has been no consistently observed relationship between HC and BPD in the third trimester with maternal CC use in pregnancy [20–23,25,26,29,35].

Ecig use is becoming more ubiquitous, especially among pregnant patients who may switch to ecigs from CC use perceiving it to be safer. However, the potential risks are largely unknown and may be similar to those associated with CC use given that most ecigs used by pregnant women contain nicotine and many other toxicants that have been implicated in negative fetal effects secondary to CC exposure [36]. Thus, it is necessary to understand how use of ecigs in pregnancy may impact fetal growth. Our pilot study aimed to examine the association between electronic cigarette exposure and fetal growth. Specifically, we investigated: are effects evident at birth, if so, how early in gestation is growth impacted, and are effects global or are only specific growth parameters impacted?

2. Materials and Methods

2.1. Participants and Procedure

Participants were drawn from women receiving prenatal care at an academic obstetric practice including patients from both the immediate semi-urban area and the larger surrounding rural region. Patients were initially eligible for study inclusion if they entered prenatal care during the study period (2018-2022), had a singleton pregnancy, were at least 18 years of age, entered prenatal care by 20 weeks gestation, and had completed the usual routine anatomy ultrasound between 18-and 22-weeks gestation per clinical guidelines, and another ultrasound with anatomical measurements taken between 30-34 weeks. An automated search of the electronic medical records resulted in a list of 1,428 women. Medical records of these women were then manually reviewed for study variables. As part of the parent study, women with different types of substance use were classified into exposure groups, along with a group of control women. Women for whom no biologic assessment of substance use was available (n=368) were automatically eliminated. A comparison of women eligible for our study with biologic assessment of substance use with those for whom this assessment was not performed indicated no significant differences on any of the factors in Table 1. However, among the women in the larger parent study, those with biologic assessment were 18% more likely to have used opiates or cannabis during pregnancy compared to those not biochemically assessed.

Table 1. Background differences between electronic cigarette users and non-users.

	Controls (n=171)	ECig Users (n=20)	P
Maternal age (yrs)	25.4 (4.8)	24.4 (4.2)	.409
Maternal race (% white, non-Hispanic)	41.5%	78.9%	.002
Maternal marital status (% single)	67.1%	100%	.003
Maternal education (% HS grad or less)	58.5%	78.9%	.083
Maternal insurance (% Medicaid/none)	68.4%	89.5%	.056
Parity	1.1 (1.2)	1.0 (1.1)	.544
Pre-pregnancy BMI	28.4 (7.1)	28.2 (7.5)	.909

Pregnancy weight gain (lb)	23.1 (12.0)	29.6 (16.2)	.226
Gestational age 1st prenatal visit (wk)	14.6 (4.0)	16.4 (5.0)	.184
Diabetes (% existing/gestational)	11/7%	0.0%	.115
Hypertension (% chronic/pregnancy induced)	17.0%	5.3%	.185
Gestational age 2nd trimester ultrasound (wk)	20.3 (1.7)	20.3 (1.4)	.919
Gestational age 3rd trimester ultrasound (wk)	34.2 (3.5)	34.0 (2.8)	.836
Gestational age at delivery (wk)	38.6 (2.2)	38.1 (3.9)	.569
Fetal gender (% male)	53.8%	63.2%	.437

Participants were classified into the ECig group if they self-reported electronic cigarette use at any point during pregnancy or at delivery. Laboratory testing was ordered as clinically indicated, with at least one lab testing available for all study participants. For most of women in the sample, this included at least one urine drug screen at entry to prenatal care (96%) and another urine drug screen at delivery (94%). Most had additional urine drug screens performed during pregnancy (90%), or had newborn cord blood testing results available (66%). All participants in the current analysis had no self-reported or biochemically confirmed alcohol, tobacco, or any other illicit drug use during pregnancy, with all laboratory testing negative for all tested substances. Additionally, study participants did not have any prescriptions for opioids, benzodiazepines, or barbiturates during pregnancy. The Control Group met all these criteria, in addition to having no positive indicator for electronic cigarette use. A total of 20 women were classified into the ECig group, and all indicated use from the beginning of pregnancy through to at least the second trimester ultrasound. A total of 171 women met criteria and were classified into the Control Group.

Following group assignment, electronic medical records were manually reviewed. Study data were abstracted onto study data collection sheets by medical student study, with regular team discussions and oversight by the senior investigator to insure data collection fidelity. Study data were entered into an electronic spreadsheet by the study coordinator, assisted by a trained undergraduate student and the medical student study investigators, with frequent checks for entry accuracy via double entry of ten percent of cases. All study procedures were approved by the Central Michigan University Institutional Review Board (study#: C-20-12 FETAL GROWTH) and included a waiver of informed consent.

2.2. Variables

The primary predictor was electronic cigarette exposure status, grouped as ECig or Control as described. No information was consistently available about amount or timing of electronic cigarette use, but all women in the ECig group reported regular use of electronic cigarettes at the time of the second trimester ultrasound examination.

Primary outcomes were derived from results of the anatomy ultrasounds performed between 18- and 24-weeks gestation (second trimester), and 30-34 weeks (third trimester), and included estimated fetal weight, femur length, and head circumference. Additional outcomes were corresponding size measurements at birth (weight, length, head circumference). Each was coded as a percentile for gestational age.

Additional data were collected to construct variables to describe the study sample and control for confounding. These included several maternal background factors: age, race/ethnicity (coded as White non-Hispanic, African American, Hispanic, and Other), marital status (coded as married vs single), highest level of education (collected as number of years but coded as high school graduate or less vs any level of post-secondary education), and medical insurance (coded as Medicaid/none vs private). Maternal medical factors collected included parity, pre-pregnancy BMI (calculated and analyzed as a continuous variable), pregnancy weight gain in pounds, gestational age in weeks/days at first prenatal medical visit, diagnosis of gestational diabetes, diagnosis of hypertension (chronic or pregnancy induced), gestational age at anatomy ultrasound in weeks/days, and infant sex.

2.3. Data Analysis

Because the study sample was intended to include all eligible electronic cigarette users, an a priori power analysis was not conducted. However, following data collection, a power analysis was performed to insure that adequate statistical power was available to answer the primary research question. Based on the group sample sizes, and using established means/standard deviations for U.S. populations, examination of estimated fetal weight revealed 80% power (at $p<.05$) to detect a 10% difference in weight at 20 weeks between the Control and ECig groups.

All assumptions of statistical tests performed were met, including equality of variances between the two unequal sized study groups. Chi-square analyses and t-tests were used to examine the association between group membership and maternal background and medical factors. Differences on the five fetal growth parameters between Control and ECig groups were examined using linear regression analyses. All background factors significantly associated with group membership at $p<.10$ were entered stepwise, followed by entry of the dichotomous electronic cigarette use group membership variable on the final step. The unstandardized regression coefficients from the final step were examined, with values interpreted as the mean difference between that exposure group and controls, and $p<.05$ considered significant. All data were managed, and all analyses were performed using IBM SPSS version 27.

3. Results

3.1. Background Differences Between Study Groups

A total of 191 participants made up the final study sample: 20 women who used electronic cigarettes during pregnancy, and 171 who did not. An analysis of background differences between the two study groups (Table 1) revealed that compared to the non-using control group, the ECig group was significantly more likely to be white, non-Hispanic and of single marital status. Differences that approached significance ($p<.10$) were that ecig users were more likely to have a high school education or less, and to be using Medicaid or no medical insurance. All four of these factors were adjusted for in controlled analyses of study outcomes.

3.2. Fetal and Newborn Size Differences Between Study Groups

Size differences between the ECig and Control groups are shown in Table 2. In the second trimester, after control for significant ($p<.10$) background differences, the ECig group had a significantly shorter average femur length than Controls, with a more than 11 percentile difference. However, there were no significant differences in estimated weight or head circumference. By the third trimester, the Ecig group was significantly smaller than the Control group on all three size measurements, with femur length now decreased by over 28 percentile points. Differences remained significant at birth, with the ECig group significantly lighter, shorter, and with a significantly smaller head circumference compared to controls.

Table 2. Adjusted¹ mean percentile size differences between those with electronic cigarette exposure compared to those without electronic cigarette exposure.

	Unstandardized Regression Coefficient (SE)	p ²
Second Trimester Ultrasound (18-22 wks)		
Estimated fetal weight	-.01 (6.5)	.499
Femur length	-11.5 (6.6)	.042
Head circumference	-4.5 (6.3)	.240
Third Trimester Ultrasound (30-24 wks)		
Estimated fetal weight	-17.2 (8.9)	.028
Femur length	-28.5 (9.3)	.001
Head circumference	-11.1(8.6)	.048
Birth		
Weight	-12.8 (6.5)	.025
Length	-19.3 (6.9)	.003

Head circumference	-13.3 (7.4)	.037
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¹ Regression coefficient controlled for maternal race, marital status, education, and insurance. ² 1-tailed test.

4. Discussion

The current study found that use of electronic cigarettes during pregnancy predicted growth deficits evident as early as the second trimester of gestation, with length impacted early, and both weight and head circumference ultimately decreased following exposure. These findings are consistent with the findings from previous animal and human studies, but also add additional insights. Several other studies report an association between prenatal ecig exposure and birthweight in humans [15–19]. We have additionally demonstrated effects on size overall, with significant relationships between exposure and both newborn length and head circumference, suggesting this exposure may not just decrease body mass, but could also impact bone growth. This is similar to what we have known for decades about the effects in utero combustible cigarette exposure, which have consistently been found to predict most anthropomorphic measurements, including length and head circumference at birth [37,38].

Our study also demonstrated that exposure to electronic cigarettes early in gestation may proximally impact fetal size, especially bone growth, as we found a relationship between exposure and femur length in the second trimester. By the third trimester, significantly decreased head circumference and overall weight were also identified among those exposed. Again, this is similar to what has been found following exposure to combustible cigarettes [2,21,23,26,28–30]. Based on our findings and preliminary work in other studies, electronic cigarettes do not appear to be a “safer” alternative to combustible cigarette use in pregnancy when considering potential impacts on fetal growth.

The current study has several strengths. Due to the use of existing data and the IRB-granted waiver of informed consent, our data were population based, representing all women in prenatal care, with minimal potential for volunteer bias, a common concern with prospective research on substance use during pregnancy. In addition, we eliminated all women who smoked combustible cigarettes or used any other substances in pregnancy, allowing us to examine the potential effects of ecigs on fetal growth independent of the known effects of other exposures. Finally, this study is the first that we know of to look at electronic cigarette use early in pregnancy in relation to specific fetal growth indices as early as the second trimester.

Despite its strengths, this study is not without limitations. While the overall population from which this sample was drawn was fairly large, the number of electronic cigarette users who did not also smoke combustible cigarettes or use any other substances was limited. While it should be noted that we did have 80% power to detect moderate effects sizes, our conclusions could certainly have been strengthened by a larger number of participants in our Ecig group. Related to this issue is the representativeness of the sample. While we excluded participants who used other substances during pregnancy in order to more cleanly look at the impact of electronic cigarettes in this smaller sample, this did mean that our participants were not completely representative of all electronic cigarette users, as a sizable percentage do use other substances. Thus, we were unable to draw any conclusions about how the effects of electronic cigarettes on fetal growth may be enhanced or even mitigated by the concurrent exposure to other substances. The generalizability of findings may also be limited due to the regional, relatively homogeneous single site sample. A further limitation of the study was the methodology, with data coming retrospectively from medical charts. Substance use is often under-reported in the medical record during pregnancy due to many factors including women not being asked, women unwilling to disclose use, and biologic testing being intermittent at best. Thus, it is very possible that some women who used electronic cigarettes were included in the control group, and that women who used other substances were included in both groups, potentially underestimating the outcomes following electronic cigarette exposure in utero. Additionally, the amount, timing, and type of in utero electronic cigarette exposure may play a role in predicting growth outcomes, however, this information was unavailable in the current study. Finally, this study

was observational in nature, and as such does not permit cause and effect conclusions. Further research is needed to address many of these limitations and add validity to the current results.

The clinical and public health relevance of our findings are important to consider. Many women, and even medical professionals, believe that ecigs may be a better alternative to combustible cigarettes during pregnancy. Based on our findings and those of other recent studies, that does not appear to be the case. Even use early in pregnancy, as we demonstrated, may cause harm. Pregnant women should be encouraged to eliminate all forms of smoking during pregnancy, and clinical advice and public health messaging should be consistent and clear in this recommendation to promote the healthiest pregnancies possible.

5. Conclusions

In this preliminary study, significant fetal size deficits were associated with prenatal electronic cigarette exposure and were evident as early as the second trimester. Differences in fetal size between pregnancies involving electronic cigarette exposure and those that did not, were larger and involved more growth parameters with increasing gestation, and by birth involved all three parameters studied: weight, length, and head circumference. Given the small sample size, additional study is needed to confirm these findings. However, this study adds to emerging data pointing to specific harms following electronic cigarette exposure in pregnancy, and suggests that e-cigarette use may not be a “safer” alternative to combustible cigarette smoking in pregnancy.

Author Contributions: Conceptualization, B.B., P.D. and K.N.; methodology, B.B., P.D. and K.N.; formal analysis, B.B.; investigation, B.B. and M.A.; resources, B.B.; data curation, P.D. and K.N.; writing—original draft preparation, B.B. and M.A.; writing—review and editing, all authors.; supervision, B.B. All authors have read and agreed to the published version of the manuscript.”

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Covenant Medical Center (C-20-12 FETAL GROWTH, original approval date 4/4/2020).

Informed Consent Statement: A waiver of informed consent was approved by the IRB due to the retrospective nature of this study.

Data Availability Statement: Restrictions apply to the availability of these data. Data were obtained from HIPAA protected medical records of Covenant Health System, and are only available directly from that organization.

Acknowledgments: The authors would like to thank Victoria Zablocki for her project coordination efforts, and the mothers who provided their medical information for this study.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. Centers for Disease Control and Prevention (US); 2014.
2. Bailey, B.A.; Kopkau, H.; Nadolski, K.; Dodge, P. Impact of in utero tobacco exposure on fetal growth: amount of exposure and second trimester fetal growth measurements. *Neurotoxicol Teratol* **2024**, *102*, 107334. doi:10.1016/j.ntt.2024.107334.
3. McEvoy, C.T.; Spindel, E.R. Pulmonary effects of maternal smoking on the fetus and child: effects on lung development, respiratory morbidities, and life-long lung health. *Paediatr Respir Rev* **2017**, *21*, 27-33. doi:10.1016/j.prrv.2016.08.005
4. Ciobanu, A.; Rouvali, A.; Syngelaki, A.; Akolekar, R.; Nicolaides, K.H. Prediction of small for gestational age neonates: screening by maternal factors, fetal biometry, and biomarkers at 35-37 weeks' gestation. *Am J Obstet Gynecol* **2019**, *220*(5), 486.e1-486.e11. doi:10.1016/j.ajog.2019.01.227
5. Ratnasiri, A.W.G.; Gordon, L.; Dieckmann, R.A. et al. Smoking during pregnancy and adverse birth and maternal outcomes in California, 2007 to 2016. *Am J Perinatol* **2020**, *37*(13), 1364-1376. doi:10.1055/s-0039-1693689

6. Tobacco and nicotine cessation during pregnancy: ACOG Committee Opinion, Number 807. *Obstet Gynecol* **2020**, 135(5), e221-e229. doi:10.1097/AOG.0000000000003822
7. Dobbs, P.D.; Lu, Y.; Maness, S. et al. Gestational women's perceptions about the harms of cigarette and e-cigarette use during pregnancy. *Matern Child Health J*, **2021**, 25(8), 1209-1220. doi:10.1007/s10995-020-03085-0
8. Vilcassim, M.J.R.; Stowe, S.; Majumder, R.; Subramaniam, A.; Sinkey, R.G. Electronic cigarette use during pregnancy: Is it harmful? *Toxics* **2023**, 11(3). doi:10.3390/toxics11030278
9. Bhattacharya, B.; Narain, V.; Bondesson, M. E-cigarette vaping liquids and the flavoring chemical cinnamaldehyde perturb bone, cartilage and vascular development in zebrafish embryos. *Aquat Toxicol* **2021**, 240, 105995. doi:10.1016/j.aquatox.2021.105995
10. Orzabal, M.R.; Lunde-Young, E.R.; Ramirez, J.I. et al. Chronic exposure to e-cig aerosols during early development causes vascular dysfunction and offspring growth deficits. *Transl Res* **2019**, 207, 70-82. doi:10.1016/j.trsl.2019.01.001
11. Cahill, K.M.; Gartia, M.R.; Sahu, S. et al. In utero exposure to electronic-cigarette aerosols decreases lung fibrillar collagen content, increases Newtonian resistance and induces sex-specific molecular signatures in neonatal mice. *Toxicol Res* **2022**, 38(2), 205-224. doi:10.1007/s43188-021-00103-3
12. Wetendorf, M.; Randall, L.T.; Lemma, M.T. et al. E-cigarette Exposure delays implantation and causes reduced weight gain in female offspring exposed in utero. *J Endocr Soc* **2019**, 3(10), 1907-1916. doi:10.1210/je.2019-00216
13. Chen, H.; Li, G.; Chan, Y.L. et al. Maternal e-cigarette exposure in mice alters DNA methylation and lung cytokine expression in offspring. *Am J Respir Cell Mol Biol* **2018**, 58(3), 366-377. doi:10.1165/rcmb.2017-0206RC
14. Wang, X.; Lee, N.L.; Burstyn, I. Smoking and use of electronic cigarettes (vaping) in relation to preterm birth and small-for-gestational-age in a 2016 U.S. national sample. *Prev Med (Baltim)* **2020**, 134, 106041. doi:10.1016/j.ypmed.2020.106041
15. Kim, S.; Oancea, S.C. Electronic cigarettes may not be a "safer alternative" of conventional cigarettes during pregnancy: evidence from the nationally representative PRAMS data. *BMC Preg Childbirth* **2020**, 20(1), 557. doi:10.1186/s12884-020-03247-6
16. Cardenas, V.M.; Cen, R.; Clemens, M.M. et al. Use of electronic nicotine delivery systems (ENDS) by pregnant women I: Risk of small-for-gestational-age birth. *Tob Induc Dis* **2019**, 17, 44. doi:10.18332/tid/106089
17. Hawkins, S.S.; Wylie, B.J.; Hacker, M.R. Associations between electronic nicotine delivery systems and birth outcomes. *J Matern Fetal Neonatal Med* **2022**, 35(25), 6868-6875. doi:10.1080/14767058.2021.1929156
18. Regan, A.K.; Bombard, J.M.; O'Hegarty, M.M.; Smith, R.A.; Tong, V.T. Adverse birth outcomes associated with prepregnancy and prenatal electronic cigarette use. *Obstet Gynecol* **2021**, 138(1), 85-94. doi:10.1097/AOG.0000000000004432
19. Regan, A.K.; Pereira, G. Patterns of combustible and electronic cigarette use during pregnancy and associated pregnancy outcomes. *Sci Rep* **2021**, 11(1), 13508. doi:10.1038/s41598-021-92930-5
20. Newnham, J.P.; Patterson, L.; James, I.; Reid, S.E. Effects of maternal cigarette smoking on ultrasonic measurements of fetal growth and on Doppler flow velocity waveforms. *Early Hum Dev* **1990**, 24(1), 23-36. doi:10.1016/0378-3782(90)90003-2
21. Vik, T.; Jacobsen, G.; Vatten, L.; Bakketeig, L.S. Pre- and post-natal growth in children of women who smoked in pregnancy. *Early Hum Dev* **1996**, 45(3), 245-255. doi:10.1016/0378-3782(96)01735-5
22. Zaren, B.; Lindmark, G.; Bakketeig, L. Maternal smoking affects fetal growth more in the male fetus. *Paediatr Perinat Epidemiol* **2000**, 14(2), 118-126. doi:10.1046/j.1365-3016.2000.00247.x
23. Lampl, M.; Kuzawa, C.W.; Jeanty P. Prenatal smoke exposure alters growth in limb proportions and head shape in the midgestation human fetus. *Am J Hum Biol* **2003**, 15(4), 533-546. doi:10.1002/ajhb.10140
24. Hanke, W.; Sobala, W.; Kalinka, J. Environmental tobacco smoke exposure among pregnant women: impact on fetal biometry at 20-24 weeks of gestation and newborn child's birth weight. *Int Arch Occup Environ Health* **2004**, 77(1), 47-52. doi:10.1007/s00420-003-0475-0
25. Pringle, P.J.; Geary, M.P.P.; Rodeck, C.H.; Kingdom, J.C.P.; Kayamba-Kay, S.; Hindmarsh, P.C. The influence of cigarette smoking on antenatal growth, birth size, and the insulin-like growth factor axis. *J Clin Endocrinol Metab* **2005**, 90(5), 2556-2562. doi:10.1210/jc.2004-1674
26. Jaddoe, V.W.V.; Verburg, B.O.; de Ridder, M.A.J. et al. Maternal smoking and fetal growth characteristics in different periods of pregnancy: the generation R study. *Am J Epidemiol* **2007**, 165(10), 1207-1215. doi:10.1093/aje/kwm014
27. Bergsjø, P.; Bakketeig, L.S.; Lindmark, G. Maternal smoking does not affect fetal size as measured in the mid-second trimester. *Acta Obstet Gynecol Scand* **2007**, 86(2), 156-160. doi:10.1080/00016340600984696
28. Prabhu, N.; Smith, N.; Campbell, D. et al. First trimester maternal tobacco smoking habits and fetal growth. *Thorax* **2010**, 65(3), 235-240. doi:10.1136/thx.2009.123232

29. Iñiguez, C.; Ballester, F.; Amorós, R.; Murcia, M.; Plana, A.; Rebagliato M. Active and passive smoking during pregnancy and ultrasound measures of fetal growth in a cohort of pregnant women. *J Epidemiol Community Health* **2012**, *66*(6), 563-570. doi:10.1136/jech.2010.116756
30. Iñiguez, C.; Ballester, F.; Costa, O. et al. Maternal smoking during pregnancy and fetal biometry: the INMA Mother and Child Cohort Study. *Am J Epidemiol* **2013**, *178*(7), 1067-1075. doi:10.1093/aje/kwt085
31. Bernstein, I.M.; Plociennik, K.; Stahle, S.; Badger, G.J.; Secker-Walker, R. Impact of maternal cigarette smoking on fetal growth and body composition. *Am J Obstet Gynecol* **2000**, *183*(4), 883-886. doi:10.1067/mob.2000.109103
32. Heil, S.H.; Higgins, S.T.; Bernstein, I.M. et al. Effects of voucher-based incentives on abstinence from cigarette smoking and fetal growth among pregnant women. *Addiction (Abingdon, England)* **2008**, *103*(6), 1009-1018. doi:10.1111/j.1360-0443.2008.02237.x
33. Lindell, G.; Maršál, K.; Källén, K. Impact of maternal characteristics on fetal growth in the third trimester: a population-based study. *Ultrasound Obstet Gynecol* **2012**, *40*(6), 680-687. doi:10.1002/uog.11125
34. Vielwerth, S.E.; Jensen, R.B.; Larsen, T.; Greisen, G. The impact of maternal smoking on fetal and infant growth. *Early Hum Dev* **2007**, *83*(8), 491-495. doi:10.1016/j.earlhumdev.2006.09.010
35. Jeanty, P.; Cousaert, E.; de Maertelaer, V.; Cantraine, F. Sonographic detection of smoking-related decreased fetal growth. *J Ultrasound Med* **1987**, *6*(1), 13-18. doi:10.7863/jum.1987.6.1.13
36. Stone, W.L.; Bailey, B.A.; Khrisha, N. The pathophysiology of smoking during pregnancy: A systems biology approach. *Front Biosci* **2014**, *E6*, 318-28. doi: 10.2741/e708.
37. Harrison, G.G.; Branson, R.S.; Vaucher, Y.E. Association of maternal smoking with body composition of the newborn. *Am J Clin Nutr* **1983**, *38*(5), 757-62. doi: 10.1093/ajcn/38.5.757.
38. Cliver, S.P.; Goldenberg, R.L.; Cutter, G.R. et al. The effect of cigarette smoking on neonatal anthropometric measurements. *Obstet Gynecol* **1995**, *85*(4), 625-30. doi: 10.1016/0029-7844(94)00437-I.

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