



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.3269826>Available online at: <http://www.iajps.com>

Research Article

**ASSESSMENT OF DETERMINANTS OF MISCARRIAGE IN
PRIMI GRAVIDA VISITING GYNAECOLOGY OUT PATIENT
DEPARTMENT**¹Dr Hafiza Maria Arshad, ²Dr Maksalmina Reshtin, ³Dr Ghulam Mujtaba¹Gujranwala Medical College Gujranwala, ²Nangarhar Medical Faculty,³Quaid-e-Azam Medical college Bahawalpur.

Article Received: May 2019

Accepted: June 2019

Published: July 2019

Abstract:

Introduction: Neonatal, prenatal and infant mortality rates are still high in developing countries despite national and international efforts to redress this problem. This study was conducted to investigate maternal knowledge and attitudes regarding the risk factors that adversely affect pregnancy outcomes and miscarriages in DHQ Gujranwala. A longitudinal study was conducted among 50 pregnant women attending antenatal clinics from start of their pregnancy to 22 weeks of gestation. Socio-economic, demographic, anthropometric, biomedical and obstetric information was collected. Results showed that, majority of the pregnant women (> 70%, n = 70) were aware of the risk factors that could adversely affect the pregnancy outcomes, however, they did not know the exact mechanisms by which the risk factors acted to cause the adverse effects. Occurrence of risk factors among pregnant women was severe anaemia - smoking, passive smoking, alcohol consumption, unmarried, under-age (< 20 years), over-age (> 35 years), history of stillbirth, history of caesarean section and history of miscarriage. A larger study should also be conducted to ascertain the association of the other risk factors with pregnancy outcomes, starting with pregnant women in their first trimester.

Materials and Methods: A longitudinal study was conducted from January 2017 to June 2017 to assess the "Determinants of miscarriages in primigravida visiting gynaecology outpatient department, DHQ hospital, Gujranwala. In this regard a comprehensive questionnaire was prepared to collect data from respondents.

Results: The potentially modifiable pre-pregnant risk factors associated with increased miscarriage risk were: age of 30 years or more at conception, underweight, and obesity. During pregnancy, the modifiable risk factors were: alcohol consumption, lifting of >20 kg daily, and night work. We estimated that miscarriages might be prevented by reduction of all these risk factors to low risk levels. Maternal age at conception and alcohol consumption were the most important risk factors.

Conclusion: Miscarriage risk is increased by multiple potentially modifiable risk factor and thus considerable proportion of miscarriages may be preventable

Key Words: Neonatal, miscarriages, primigravida, modifiable

Corresponding author:**Dr. Hafiza Maria Arshad,**

Gujranwala Medical College Gujranwala.

QR code



Please cite this article in press Hafiza Maria Arshad et al., *Assessment Of Determinants Of Miscarriage In Primi Gravida Visiting Gynaecology Out Patient Department.*, Indo Am. J. P. Sci, 2019; 07[07].

INTRODUCTION:

Miscarriage is the most common type of pregnancy loss, according to the American College of Obstetricians and Gynaecologists (ACOG). Studies reveal that anywhere from 10-15% of all clinically recognized pregnancies will end in miscarriage. Miscarriage is the loss of baby before it was able to survive independently outside the womb of mothers. It usually occurs in 20-24 weeks of gestation.¹

Miscarriage is a major public health problem across the globe due to the higher incidence and severity of its complications such as severe per vaginal bleeding, incomplete miscarriage, septic miscarriage, ill health, infertility and death of the woman. It is sometimes caused by trauma to the abdomen. The degree of force, if severe, can cause serious internal injuries without necessarily succeeding in miscarriage². A woman who is pregnant for the first time is known as primigravida. The present study is designed to determine the causes of miscarriage in primigravida. For women in their childbearing years, the chances of having a miscarriage can range from 10-25%, and in most healthy women the average is about a 15-20% chance. An increase in maternal age affects the chances of miscarriage. Women under the age of 35 yrs. old have about a 15% chance of miscarriage. Women who are 35-45 yrs. old have a 20-35% chance of miscarriage. Women over the age of 45 can have up to a 50% chance of miscarriage. A woman who has had a previous miscarriage has a 25% chance of having another (only a slightly elevated risk than for someone who has not had a previous miscarriage).

The definition by IPAS (1991) is a comprehensive definition which is miscarriage, also known as spontaneous abortion, is the unintentional expulsion of an embryo or foetus before the 20th to 22nd week of gestation. A pregnancy that ends before 37 weeks of gestation resulting in alive-born infant is known as a "premature birth" or a "preterm birth".³ Premature births and stillbirths are generally not considered to be miscarriages although usage of these terms can sometimes overlap. Only 30 to 50% of conceptions progress past the first trimester⁴. The vast majority of those that do not progress are lost before the woman is aware of the conception. Many pregnancies are lost before medical practitioners have the ability to detect the presence of an embryo. Between 15% and 30% of known pregnancies end in clinically apparent miscarriage, depending upon the age and health of the pregnant woman.⁵

The most common cause of spontaneous miscarriage during the first trimester is chromosomal abnormalities of the embryo/foetus, accounting for at least 50% of

sampled early pregnancy. Other causes include diseases such as lupus erythematosus, diabetes mellitus, other hormonal problems, infection, and abnormalities of the uterus. Advancing maternal age and a patient history of previous spontaneous miscarriages are the two leading factors associated with a greater risk of spontaneous miscarriage can also be caused by accidental trauma. According to Chicago Encyclopaedia Britannica (2009) environmental factors include all aspects of the relationship between host and health and the effects of hazardous biological and chemical agents on human health. Some of the environmental factors associated with miscarriage are excessive alcohol and coffee consumption, cigarette smoking including passive exposure to smoke, stress and malnutrition.⁶ Environmental pollutants and radiation can also predispose to miscarriage. However, this research seeks to also identify whether this variable is linked to factors contributing to miscarriages of the patients who are reporting to the Reproductive Health Care Clinic.

The causes of miscarriage in most cases remain unknown but can be associated with maternal or local disorders of the genital tract and foetal causes. Recurrent miscarriage is defined as the loss of three or more consecutive pregnancies (Stirrat 2005). This problem affects 1% of all women globally. The risk of further miscarriage increases with each pregnancy loss. Factors associated with recurrent miscarriage include genetic causes, immunological factors, and hyper secretion of luteinising hormone, infection and structural abnormalities.⁷

Threatened miscarriages: Some degree of early pregnancy are accompanied by uterine bleeding, cramping or lower backache. The cervix remains closed. This bleeding is often the result of implantation. Inevitable or Incomplete Miscarriage: Abdominal or back pain accompanied by bleeding with an open cervix. Miscarriage is inevitable when there is a dilation or effacement of the cervix and/or there is rupture of the membranes. Bleeding and cramps may persist if the miscarriage is not complete.

Completed miscarriage: It is when the embryo or products of conception have emptied out of the uterus. Bleeding should subside quickly, as should any pain or cramping. A completed miscarriage can be confirmed by an ultrasound or by having a surgical curettage performed.

Missed miscarriages: Women can experience a miscarriage without knowing it. A missed miscarriage is when embryonic death has occurred but there is not any expulsion of the embryo. It is not known why this

occurs. Signs of this would be a loss of pregnancy symptoms and the absence of foetal heart tones found on an ultrasound.

Recurrent miscarriages (RM): Defined as 3 or more consecutive first trimester miscarriages. This can affect 1% of couples trying to conceive.⁸

LITERATURE REVIEW:

Two reviewers independently searched the Pub Med database for articles published between 1956 and August 31, 2011, relevant to smoking and risk of adverse pregnancy outcomes. The search terms were (“smoking” OR “tobacco”) AND “pregnancy.” From the chosen articles, those relevant to miscarriage or perinatal death were selected for inclusion and/or review of references. We then conducted manual searches by checking references of the articles identified in the Pub Med searches. The articles referenced by all relevant articles (original articles, reviews, and letters) were searched by at least 1 reviewer, and the articles referenced by included articles and all Surgeon General reports regarding tobacco and health were searched by 2 reviewers. Disagreements on final inclusion status were resolved by discussion.⁸In a cohort of pregnant women without overt thyroid dysfunction, the risk of child loss increased with higher levels of maternal TSH. Maternal FT4 concentrations and child loss were not associated.⁹The relation between heavy and inconvenient working load and the outcome of pregnancy was studied among women. A slightly, but not significantly, increased risk of miscarriage was found in women who worked irregular hours or rotating shifts compared with women who worked only during the day.¹⁰One recent review article cited more than 200 papers. The problem is that women who drink more coffee than most nearly always differ from other pregnant women in other ways too. They are more likely to smoke, for one thing, which makes it difficult to decide what is causing what. Miscarriage risk is 67% lower with 30-31 days cycles, 60% less likely after long menstrual bleeds Obesity is associated with increased risk of first trimester and recurrent miscarriage. This was a nested case-control study. The study population was identified from a maternity database. Obese [body mass index (BMI) >30 kg/m²] women were compared with an age-matched control group with normal BMI (19–24.9 kg/m²). Only primiparous women were included in the study to avoid including the subject more than once, and to be able to correctly identify recurrent miscarriages. The prevalence of a previous history of early (6–12 weeks gestation), late (12–24 weeks gestation) and recurrent early miscarriages (REM) (more than three successive miscarriages <12 weeks) was compared between the

two groups. A total of 1644 obese and 3288 age-matched normal weight controls with a mean age of 26.6 years [95% confidence interval (CI) 26.5–26.7] were included in the study. The risks of early miscarriage and REM were significantly higher among the obese patients (odds ratios 1.2 and 3.5, 95% CI 1.01–1.46 and 1.03–12.01, respectively; P = 0.04. Obesity is associated with increased risk of first trimester and recurrent miscarriage.¹¹

Spontaneous miscarriage affects 12–15% of all pregnancies.¹² Eighty percent of miscarriages occur before 12 weeks of gestation, and the majority are due to chromosomal abnormalities.⁸Our figures from this study population are consistent with previously published data. In another study conduction on effects of glycemic control. And effect on outcomes of pregnancy suggested that Patients with higher HbA1c were older had significantly higher blood pressure, proteinuria and were multiparous. They had significantly shorter gestational periods, more preterm labor more perineal tears, more miscarriages, and more operative deliveries. Psychological stress and its emotional concomitants, commonly labeled “distress,” influence health primarily through health-impairing behaviors and physiological responses that challenge vascular, immune, metabolic, or neuroendocrine functioning.¹³ There is a growing body of evidence that prenatal maternal distress adversely affects birth outcomes through these mechanistic pathways, even when pregnancy is subjectively rated as only “somewhat” distressing.¹⁴ Prenatal distress has been associated with negative perinatal outcomes including spontaneous abortion, structural malformations, preeclampsia, low birth weight, and preterm delivery and with relatively long-term outcomes, including unfavorable neuroendocrine regulation and impaired neurobehavioral development in children.¹⁵

OBJECTIVES:

Objective of this research was to give suggestions and recommendations for prevention and control of miscarriages in primigravida.

To assess the knowledge of patients reporting to DHQ, Gujranwala, about miscarriage and its risk factors.

To identify practices by patients, that may contribute to increased risk of miscarriages.

MATERIALS AND METHODS:

General: Methodology is the theoretical and systematic analysis of the methods applied to the field of study.

Study design: We conducted a follow-up study based on pregnancies enrolled in the DHQ, Gujranwala between January 2017 to June 2017. The recruitment of participants occurred in connection with the antenatal visit at the general practitioner, which in Gujranwala normally takes place shortly after recognition of the pregnancy. The pregnant women provided informed consent, and permission was obtained before initiation of the study.

Place of study: The place of study was OPD of DHQ/UTH Gujranwala. It is a prominent city of Gujranwala district of Punjab. It is the fourth most populated city of Pakistani metropolitan area and is one of the fastest developing city of Pakistan. According to 1998 census, the population of district is 3,400,940 of which 50.101% is urban while remaining are rural.

Study population: We included all pregnancies with information on risk factors for miscarriage that was provided either in an interview during pregnancy (past miscarriage) or after a miscarriage. We set some further exclusion criteria: hydatid form mole and ectopic pregnancies, pregnancies enrolled in the DHQ at 22 gestational weeks or later, and pregnancies with no information on gestational age.

Duration of study: The study was conducted from January 2017 to June 2017.

Sampling technique: Simple Random Sampling was used for the selection of sample among miscarriage patients.

Sample Size: 50 women visiting Gynaecology Department, DHQ Hospital were included in sample.

Sample selection:

Inclusion criteria: Females who had miscarriage in primigravida visiting OPD at DHQ Gujranwala were included in the study sample.

Exclusion Criteria: Females who had miscarriage in second or third trimester, pregnant women and patients with any other gynaecological cause visiting OPD at DHQ Gujranwala were excluded from the study.

Ethical issues: Formal written consent and permission had been taken from patients and superintendent, DHQ Gujranwala to conduct the study. It was insured that this data will be kept confidential.

Data Collection: A semi structured questionnaire was prepared by the researcher. The females who had miscarriage in primigravida visiting OPD, Gujranwala

were face to face interviewed and the data was noted on questionnaire.

Data Analysis: The data collected was analyzed thereafter, using SPSS software version 2.0.

RESULTS AND ANALYSIS:

A self-administered questionnaire has been got filled from 100 females who had miscarriage in primigravida, visiting OPD at DHQ Hospital, Gujranwala. The information has been gathered regarding the bio data of patient and the determinants of miscarriage. The analysis is given in the following tables, figures, charts and detailed descriptions.

Table 5.1: Age distribution of the sample

Age at miscarriage	Frequency	Percentage
20-25	10	20%
25-30	14	28%
30-35	26	52%

Females between age 20-25 had miscarriage 20%, 25-30 were 28% and between 30-35 were 52%.

Table 5.2: Population distribution of Sample

Residency	Frequency	Percentage
Rural	38	76%
Urban	12	24%

The females living in rural areas were 76% and urban population was 24% in given sample.

Table 5.3: Literacy prevalence in sample

Literacy Rate	Frequency	Percentage
Middle	4	8%
Matriculation	11	22%
Inter	26	52%
Graduation	9	18%

Females with education till middle were 8%, with matriculation were 22%, inter were 52% and graduated were 18%.

Table 5.4: Gestational age

	Frequency	Percent	Valid Percent	Cumulative Percent
1st trimester	39	77.6	77.6	77.6
Valid 2nd trimester	11	22.4	22.4	100.0
Total	50	100.0	100.0	

Percentage of Miscarriages in 1st trimester is 77.6% and percentage of Miscarriages in 2nd trimester: 22.4% .

Table 5.5: Hypertension

	Frequency	Percent	Valid Percent	Cumulative Percent
No	41	78.1	78.1	78.1
Valid Yes	9	21.9	21.9	100.0
Total	50	100.0	100.0	

DISCUSSIONS:

In this small hospital confined case control study, we found that majority of the miscarriages were preventable by modification of multiple risk factors to low risk levels. Maternal stress and tobacco consumption were most common determinants of miscarriage in primigravida. Our study extends the relative risk approach used in most previous studies by estimating determinants of miscarriage attributed to multiple modifiable risk factors. Tobacco and drugs like caffeine (coffee) use are some of the lifestyle behaviors that have been reported to cause poor pregnancy outcome i.e; miscarriages in primigravida. These findings are consistent with our study too.¹⁷Low education level has indirect effects on the understanding of nutrition and food aspects as well as improvement of the socio-economic conditions: Maternal education level therefore influences the food choices and feeding patterns of family members. Majority of the women in this study had attained above primary level education so unlike previously done studies, in our study, no significant relationship was established between this variable and miscarriage.¹⁸Contrary to the present study, smoking was found to explain relatively high proportions of miscarriage in some previous studies.¹⁹ In a more recent cohort study; however, no association between smoking and miscarriage was identified. We believe that our finding of maternal stress association with miscarriage is quite reliable and there is a direct relation between the two, about which the data in previous studies is not found up to satisfactory levels.²⁰²¹Mother's age at miscarriage is also an important risk factor for miscarriage in primigravida, according to previous studies²² but our study is not consistent with this finding as majority of our samples included females with primigravida miscarriage in early and late twenties due to early adult marriages in this region. Gestational Age is also important determinant in primigravida miscarriage with majority of miscarriages being occurring in first trimester attributed to maternal and chromosomal aberrations.²⁴

CONCLUSION:

This study adds an important perspective to the miscarriage research by suggesting that some miscarriages are preventable. A future study based on similar methods but using relative risk estimates

obtained from meta-analysis would be a preferred approach to estimate PAFs. Factors such as tea/coffee consumption, mental stress, and oral contraceptives should be modified during pregnancy to improve the outcomes and prevent miscarriages in primigravida. Age at the time of miscarriage is found to be early twenties in our study, according to social settings of the area. If our findings are supported by future prospective cohort studies, they may be used in a prevention strategy against miscarriages.

RECOMMENDATIONS:

That said a healthy lifestyle before and during pregnancy may help produce a safe and healthy output of pregnancy. In the light of our research and previously done studies, here are some recommendations:

If you're not already pregnant: Schedule a pre-conception visit with your gynecologist. She'll review your medical history, ask about your lifestyle, perform an annual exam (if you're due for one), and take blood samples to check for blood type, Rh factor. If you haven't been vaccinated against these infectious diseases, now's the time to get your shots.

Eat a well-balanced diet: A well-balanced, healthy diet is the best way to get the vitamins and nutrients your body needs to nourish your baby, studies have found that loading up on a variety of fresh fruits and veggies every day can significantly lower your odds of having a miscarriage.²⁵

Exercise in moderation: You should continue your usual exercise routine once you're pregnant. The key is moderation: Some research indicates that seven hours or more of high-impact exercise a week while pregnant could greatly increase your risk of miscarriage.²⁶

Limit caffeine: Some doctors suggest moms-to-be restrict their intake to no more than 200 milligrams a day, or roughly two 6-ounce cups of coffee, tea, or other caffeinated beverage. But to be on the safe side, ask your ob-gyn what she recommends.²⁷

Avoid drugs, smoking, and alcohol.

Get a handle on stress: Besides improving your overall mood, staying relaxed may also help the health of your pregnancy. In one study, women who said they felt happy relaxed, and in control were 60 percent less likely to have a miscarriage.²⁷

Get your blood sugar under control (if you have diabetes): Elevated blood sugar can lead to fetal malformation and a subsequent loss. So it must be avoided.²⁷

Ask if you should take low-dose aspirin: Although a recent National Institutes of Health study found that, in general, low-dose aspirin did not appear to prevent miscarriage in women with one or two prior pregnancy losses, it did appear to be effective for a smaller subset of women.²⁸

LIMITATIONS:

Our study also has some limitations. Although we have early recruitment to the DHQ, Gujranwala, the majority of women were recruited after the gestational age where miscarriage is most common; this explains why the observed proportion of miscarriages was only 3.5%, in contrast to the 11–14% of all pregnancies which are expected to end in miscarriages.²⁹

As excluding subjects from survival analysis on the basis of future events would bias results, we allowed women whose pregnancy ended in an induced abortion to contribute with risk time until event. Censoring due to induced abortion was likely to represent fetuses with systematic reduced changes of survival. However, the sensitivity analysis indicated that the handling of induced abortions did not seem to affect the conclusions. Another limitation was that the majority of the women who experienced a miscarriage were interviewed after the event, which could have introduced recall bias.

The validity of the PAF²⁹ estimates depends on some methodological assumptions, i.e., causality, non-confounding and well-defined interventions, and these requirements were not necessarily fulfilled for all risk factors in our analysis. The associations between amount of exercise during pregnancy, coffee consumption during pregnancy, previously diagnosed genital diseases and miscarriage were likely to be biased because of systematic differences in recall of exposure and residual confounding; consequently, we defined no prevention scenarios regarding these factors. However, even for the risk factors included in the final analysis we cannot tell from this observational study whether the associations are causal.

This is partly because confounding or reverse causality could have resulted in biased risk estimates, except from those presented for maternal age. How easy it is to modify maternal age at the time of conception may be questioned. Although factors such as having a partner, education, social network, and the norms in the society play an important role to the modifiable aspects of this risk factor, we think that information about increased chances of having a successful pregnancy in a relatively young age as well as the society's facilitation of parenthood at an early age by creating better opportunities for combining education or participation

in the working force and childbearing are important perspectives in future miscarriage research. Also, the women in the DHQ, Gujranwala are not a representative sample of all pregnant women in Gujranwala.

REFERENCES:

1. *Current Obstetric & Gynecologic Diagnosis & Treatment* Ninth Ed. DeCherney, Alan H., et al, Ch. 14. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2006 Feb 23]. Pregnancy Loss; [updated 2006 Feb 22; reviewed 2006 Feb 7; cited 2006 Feb 23].
2. Kaiser Permanente. Miscarriage: Regional Health Education. [E-Handout]. #1045-E, Revised 6-11: the Permanente Medical Group, Inc; 2007. [cited 2012 Apr 16] Available From URL: <http://www.permanente.net/homepage/kaiser/pdf/15284.pdf>
3. Garcia-Enguidanos A, Calle ME, Valero J, Luna S, Dominguez-Rojas V. Risk factors in miscarriage: a review. *Eur J ObstetGynecolReprodBiol* 2002;**102**:111–19.
4. Elias, Sherman (2007). "51. *Legal and Ethical Issues in Obstetric Practice*". In [Gabbe, Steven G.](#); [Niebyl, Jennifer R.](#); [Simpson, Joe Leigh](#). *Obstetrics: Normal and Problem Pregnancies*. (5 ed.). [Churchill Livingstone](#). p. 669.
5. *Systematic Review and Meta-Analysis of Miscarriage and Maternal Exposure to Tobacco Smoke During* L. Pineles, Edward Park, and Jonathan M. Samet *Am J Epidemiol*. 2014 Apr 1; 179(7): 807–823 Published online 2014 Feb 10. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3969532/>)
6. H. Lashen K. Fear D.W. Sturdee *Human Reproduction*, Volume 19, Issue 7, 1 July 2004, Pages 1644–1646, <https://doi.org/10.1093/humrep/deh277> Published: 01 July 2004 Article history.
7. <http://oem.bmj.com/content/46/6/393.short> *Coffee and pregnancy*, *BMJ*. 2007 Feb 24; 334(7590): 377. Edmund Hey: ku.oc.tenysae@yehs.
8. *Menstrual Cycle Characteristics: Associations With Fertility and Spontaneous Abortion* Small, Chanley M.*; Manatunga, Amita K.†; Klein, Mitchel‡; Feigelson, Heather S.§; Dominguez, Celia E.¶; McChesney, Ruth||; Marcus, Michele* *Epidemiology: January 2006 - Volume 17 - Issue 1 - pp 52- .*
9. *Glycemic control and pregnancy outcomes in patients with diabetes in pregnancy: A retrospective study* BadurudeenMahmoodBuhary, OhoudAlmohareb, [...], and MussaAlmalki *Indian J EndocrinolMetab*. 2016 Jul-Aug; 20(4): 481–490. doi: 10.4103/2230-8210.183478Badurud

- eenMahmoodBuhary,
OhoudAlmohareb,NajiAljohani, Saad H. Alzahrani,
SamerElkaissi,SuphiaSherbeeni,
AbdulrahmanAlmaghamasi, andMussaAlmalki.
10. Dunkel-Schetter, Gurung, Lobel, &Wadhwa, 2001; Lobel, 1994; Lobel, Hamilton, &Cannella, 2008.
 11. Dewey, K.G. & Cohen, R.J. (2007) Does birth spacing affect maternal or child nutritional status? A systematic literature review. *Maternal and Child Nutrition* 3, 151-173.
 12. Hinderaker, S.G., Olsen, B.E., Bergsjø, P., Lie, R.T., Gacheka, P. &Kvale, G. (2001) *Anaemia in pregnancy in the highlands of Tanzania. ActaObstetriciaetGynecologicaScandinavica.* 80, 18 – 26.
 13. Children (Mulder et al., 2002; Van den Bergh &Marcoen, 2004; Van den Bergh, Mulder, Mennes, & Glover, 2005).
 14. from Wikipedia a free encyclopedia.
 15. Wilcox AJ. *Miscarriage. Infertility and Pregnancy: An Epidemiological Perspective* 1stedn. Oxford: Oxford University Press; 2010 pp. 149-63
 16. Hirsch, L. (2008) What is Apgar score. [http://kidshealth.org/parent/pregnancy_newborn/apgar_score.html] site visited on 4/2/2009.
 17. IOM (2009) Institute of Medicine of the National Academy (2009). *Weight gain during pregnancy: Re-examining the guidelines.* Website: www.nap.edu/pregnancyweightgain. Site visited 08/09/2009.
 18. Ness RB, Grisso JA, Hirschinger N, Markovic N, Shaw LM, Day NL, et al. *Cocaine and tobacco use and the risk of spontaneous abortion.* N Engl J Med 1999;340:333–9.
 19. Chatenoud L, Parazzini F, Di CE, Zanconato G, Benzi G, Bortolus R, et al. *Paternal and maternal smoking habits before conception and during the first trimester: relation to spontaneous abortion.* Ann Epidemiol 1998;8:520–6.
 20. Armstrong BG, McDonald AD, Sloan M. *Cigarette, alcohol, and coffee consumption and spontaneous abortion.* Am J Public Health 1992;82:85–7.
 21. Wisborg K, Kesmodel U, Henriksen TB, Hedegaard M, Secher NJ. *A prospective study of maternal smoking and spontaneous abortion.* ActaObstetGynecolScand2003; 82:936–41.
 22. Baba S, Noda H, Nakayama M, Waguri M, Mitsuda N, Iso H. *Risk factors of early spontaneous abortions among Japanese: a matched case-control study.* Hum Reprod 2011;26:466–72. Am J Epidemiol 1996;144:989–96.
 23. Madsen M, Jorgensen T, Jensen ML, Juhl M, Olsen J, Andersen PK, et al. *Leisure time physical exercise during pregnancy and the risk of miscarriage: a study within the Danish National Birth Cohort.* BJOG 2007;114:1419–26.
 24. Zhang H, Bracken MB. *Tree-based, two-stage risk factor analysis for spontaneous abortion.* Am J Epidemiol 1996;144:989–96.
 25. Weigel RM, Weigel MM. *Nausea and vomiting of early pregnancy and pregnancy outcome. A meta-analytical review.* Br J Obstet Gynaecol 1989;96:1312–8.