RISK FACTORS FOR PLACENTAL ABRUPTION:

A CASE-CONTROL STUDY

Master of Public Health Integrating Experience Project

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by

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LIST OF ABBREVATIONS

ANC	Antenatal Care
BP	Blood Pressure
BMI	Body Mass Index
CI	Confidence Interval
FTBL	First trimester vaginal bleeding
GA	Gestational age
“GN”MC	Medical Center “Grigor Narekatsi”
IPOG	Institute of Perinatology, Obstetrics and Gynecology
MOH	Ministry of Health
NIH	National Institute of Health
OR	Odds ratio
PlAb	Placental abruption
RCMCHP	Research Center of Maternal and Child Health Protection
SD	Standard Deviation
VBAC	Vaginal birth after Cesarean Section
VIF	Variance Inflation Factor

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ABSTRACT

Background. Placental abruption (PlAb) is a complete or partial detachment of the placenta before child's delivery. PlAb complicates about 1% of pregnancies and is a leading cause of vaginal bleeding in the second half of pregnancy, and an important cause of perinatal mortality and morbidity. The aim of this study was to investigate the risk factors of placental abruption, and measure the association between first trimester vaginal bleeding (FTBL) and placental abruption at pregnancy termination.
Methods. A case-control study was conducted with 83 cases and 166 controls identified among 7,861women who delivered at tertiary and secondary levels three maternities in 2010 in Yerevan. Stata 10 statistical software was used for data analysis. Clinical and demographic variables were compared between the groups. Simple and multivariate logistic regression analyses were applied to identify independent risk factors.
Results. After adjusting for confounders (age, body mass index, education, socioeconomic condition), the risk of developing PlAb was more than three times higher among women with three and more days of the FTBL (OR 3.6; p=0.01). The odds of developing PlAb was more than four times higher among women with preeclampsia (OR 4.6; p=0.001). A statistically significant interaction was detected between preeclampsia and maternal age. While there was no association between maternal age and PlAb among women with normal blood pressure, among women with preeclampsia each year increase in age was associated with 20% increased risk of PlAb. Women with less than 13 kg weight gain during pregnancy have twice higher risk of developing PlAb compared with those who gained 13 kg and more (OR 2.2; p=0.014). The similar association was found between higher education (>13 years) and PlAb (OR 2.1; p=0.018). Sleeping on back position increases the risk of PlAb by 20% (OR 1.2; p=0.021).
Conclusions. Study has demonstrated that first-trimester vaginal bleeding is an independent risk factor for placental abruption, and patients who reported three and more days of the first trimester vaginal bleeding showed an increased risk of placental abruption.

INTRODUCTION

Background

Placental abruption is a complete or partial detachment of the placenta before child's delivery. It is one of the most dangerous complications during pregnancy and labor(1). Placental abruption complicates about 1% of pregnancies and is a leading cause of vaginal bleeding in the latter half of pregnancy. It is also an important cause of perinatal mortality and morbidity. The maternal effect of abruption depends primarily on its severity, whereas its effect on the fetus is determined both by its severity and the gestational age at which it occurs. Results of the study conducted by Oyelese and Ananth showed that placental abruption involving more than 50% of the placenta is frequently associated with fetal death(2). The most severe complications of placental abruptions with large detachment area are fetal death, severe maternal shock, disseminated intravascular coagulopathy, and renal failure(3). Compared with controls, newborns in the placental abruption group are born earlier, have lower birthweight, are more often growth restricted, have lower Apgar scores, and consequently more often require special care(4).

The most common clinical symptoms of placental abruption are bleeding and pain but the clinical picture can vary from almost asymptomatic, in which the diagnosis is made retrospectively by inspection of the placenta at delivery, to massive abruption leading to fetal death and severe maternal morbidity. The diagnosis is always clinical(1;2), and the presence of retroplacental clots remained the only most common finding (77.1%) among clinically diagnosed cases. The only histological finding associated with abruption is placental infarctions. Elsasser et al. found that the concordance between clinical and pathohistologic criteria for abruption diagnosis is poor(5).

The etiology of placental abruption is not fully understood. The key mechanisms causing placental abruption are impaired placentation, placental insufficiency, intrauterine hypoxia, and uteroplacental underperfusion. Abruption results from a rupture of maternal decidual artery causing dissection of the decidual-placental interface. Acute vasospasm of small vessels may precede abruption. The trophoplastic invasion in the spiral arteries and subsequent early vascularization may be defective. Inflammatory process in decidual vessels is another possible mechanism for placental abruption(1;2;6).

Despite high awareness of possible severe complications, placental abruption still remains unpredictable and unpreventable(1). Current antepartum methods of detecting uteroplacental problems, including Doppler ultrasonography, are not effective in prenatal prediction of placental abruption(7-9).

Several studies tried to identify risk factors for the development of placental abruption. Statistically significant risk factors for abruption include prior abruption, smoking, trauma (10;11), hypertensive disorders of pregnancy, advanced maternal age, preterm premature rupture of the membranes, intrauterine infections, and hydramnios(2;6;12-16). Multiparity, unbooked status, rural residence, maternal anemia, malpresentation (non-vertex presentation), and back sleeping position during pregnancy are additional risk factors(14-18).

Many studies indicate the association between bleeding in the first trimester of pregnancy and placental abruption in the second and third trimesters(19-22). Norman et al. revealed that the incidence of placenta previa (OR 1.62; 95% CI 1.19, 2.22) and placental abruption (OR 1.46, 95% CI 1.00, 2.14) are higher among women with first trimester bleeding(23).

A case-control study conducted in Finland by Tikkanen et al, tried to find out whether short-term maternal health outcomes differ by infant sex in cases with placental abruption. The results showed that placental abruption occurred earlier in pregnancy with male fetal sex but otherwise the outcomes were similar(4).

To evaluate the risk of placenta previa and placental abruption in singleton, second pregnancies after a cesarean delivery of the first pregnancy, a total of 5,146,742 singleton second pregnancies were analyzed by a team of researchers using a retrospective cohort study design. The result of the analysis showed that Cesarean section for the first live birth is associated with a 47% increased risk of placenta previa and 40% increased risk of placental abruption in second pregnancy with a singleton(24;25).

Some studies tried to find out the role of nutritional status during pregnancy as a predictive factor for placental abruption. In two studies obesity was associated with reduced risk for placental abruption when the weight gain during pregnancy was moderate, while the maternal underweight status before pregnancy was associated with placental abruption. Researchers are hopeful that this risk might be reduced with adequate weight gain during pregnancy(26;27).

The effect of hypertension on the risk of placental abruption varies by the specific type of hypertensive disorder during pregnancy. Chronically hypertensive women compared to normotensives had no increased risk of abruption (RR 1.4; 95% CI 0.5-3.6), while women whose pregnancies were complicated by severe pre-eclampsia (RR 3.8; 95% CI 2.1-6.9), and chronic hypertension with superimposed pre-eclampsia (RR 2.8; 95% CI 1.2-6.3) are at higher risk of developing placental abruption(16).

Situation in Armenia

We did not find any official source of information about incidence of placental abruption in Armenia. PlAb is not among indicators reported by facilities to the Ministry of Health (MOH) or National Institute of Health (NIH). All maternity homes and obstetrical departments within medical centers report the total number of cases with different types of obstetrical hemorrhages (placental abruption, placenta previa, postpartum hemorrhage) together. No one systematically collects information on placental abruption separately from other causes of obstetrical hemorrhages. We could not find any published investigations of the risk factors of PlAb in Armenia.

Aims and Research Questions of Study

The aims of the study are:

- To identify risk factors of placental abruption among women living in Armenia
- To identify associations between risk factors of placental abruption in Armenia
- To measure the association between first trimester vaginal bleeding and placental abruption at pregnancy termination

The research questions are:

- What are the risk factors of placental abruption?
- Is there any association between the first trimester vaginal bleeding and the risk of placental abruption after controlling for confounders?
- Are there any associations between different risk factors of PlAb?

METHODS

Study Design

To obtain the answers to the research questions a case-control study was conducted. The case-control design allows a less expensive investigation for risk factors of rare conditions within a short-time period. Also, this method is applicable for this study because it allows to consider multiple factors and test many hypotheses(28).

Study Population

The study population includes women who gave birth in selected tree facilities in 2010 in Yerevan. Record revision was conducted in Institute of Perinatology, Obstetrics, and Gynecology (IPOG), Research Center of Maternal and Child Health Protection (RCMCHP), and Medical Center "Grigor Narekatsi" ("GN"MC). Maternity homes and obstetrical department of medical center were selected by convenience. Out of all 20797 deliveries that took place in all maternity homes in Yerevan in 2010 more than one third (37.8%) of deliveries took place in these three facilities: IPOG, RCMCHP, and "GN"MC. Table 1 presents numbers and percentages of vaginal births, cesarean sections and placental abruptions per each facility.

Definition of Cases

Cases were women living in Yerevan that were diagnosed with placental abruption at singleton pregnancy termination, regardless of the outcome for woman or child in 2010.

Definition of Controls

Controls were women living in Yerevan that gave birth in the same chosen maternity homes without placental abruption in diagnosis at singleton pregnancy termination in 2010.

Exclusion Criteria

Exclusion criteria for both cases and controls were the absence of contact information, inability to speak Armenian, and being diagnosed with multiple pregnancies. The additional exclusion criterion for cases in final analysis was the diagnosis of placental abruption without confirmation during telephone interview.

Sample Size

The sample size was calculated using the formula for 10% difference in the proportion of the first trimester vaginal bleeding, assuming the ratio of controls to cases as 2:1 with the level of significance 0.05 and power 0.8 using Epi Info statistical software. Using these parameters, 82 cases and 164 controls were required to detect a difference of 10% in the first trimester bleeding(29).

$$m = \frac{\left[c_{\propto/2}\sqrt{(r+1)\bar{P}\bar{Q}} - c_{1-\beta}\sqrt{rP_1Q_1}\right]^2}{r(P_2-P_1)^2} = 82$$

The power analysis showed that the actual power was bigger (0.87) than estimated power (0.80) for the main independent variable FTBL.

Data Collection

Data collection was conducted during the period from February 21 to March 22, 2011. To get permission from hospitals, support letters were sent to head doctors of four maternity homes and medical centers. From three of them permission was received. Only the administration of "Shengavit" MC did not allow the records revision in their facility. After getting the permission from the heads of the three facilities the study used medical records of deliveries in 2010 to identify the study population. We extracted the contact information (names and telephone number) and necessary clinical data of women from medical records.

We selected all patients with diagnosis of placental abruption (ICD-10 O45.0, O45.8, and O45.9) among a total of 7861 deliveries during 2010 from three maternity houses and obstetrical departments in Yerevan including both tertiary and secondary levels of obstetrical care in Yerevan.

Women who delivered after 22 weeks of gestation or having a newborn weighing at least 500g were included in the analyses. The duration of the gestation calculated from the last menstrual period was confirmed based on ultrasound examination and child's weight at delivery. The information from delivery records with relevant clinical data was collected from the hospitals using specially developed record revision form (Appendix 1). The diagnosis of placental abruption was made by physicians based on clinical symptoms and findings on ultrasound examination, and was later rechecked during telephone interview.

The control group consisted of the women who had no evidence of placental abruption at pregnancy termination. The study selected controls using the following principle: after selecting each case, two controls that delivered in the same maternity before and after a woman with placental abruption were selected.

Both cases and controls were interviewed by telephone using specially developed questionnaire to obtain the missing data and check information presented in records. Telephone interviews were conducted by a specially trained female interviewer. The mean duration of telephone interviews was 7 minutes with duration range from 5 to 10 minutes.

Study Instrument

The same interviewer-administered structured questionnaire was used during the telephone interviews with both cases and controls (Appendix 2). The student investigator developed the questionnaire. The questionnaire consists of 29 mainly close-ended questions. It

includes the following main domains: anthropometric and socio-demographic characteristics, reproductive history, blood group and Rhesus factor, blood pressure, smoking, working habits, and details of the index pregnancy.

Before data collection the instrument was pre-tested among 10 women who delivered in 2010 (3 cases and 7 controls) through telephone interviews. Based on the pre-test results some changes were made related to questions about sexual life during pregnancy.

Study Variables

The dependent (outcome) variable of the study was placental abruption mentioned in final clinical diagnosis in the delivery record form and further confirmed by telephone interview. Independent variables were: age, level of education, parity, marital status, socioeconomic condition (SEC), woman's blood group and Rhesus factor, employment status of a woman during pregnancy, smoking during pregnancy, exposure to secondhand smoke, history of early pregnancy bleeding, history of previous placental abruption and cesarean section, BMI, progestogens used during pregnancy, sleeping position, and hypertension during pregnancy. The main potential risk factors related to the course of the index pregnancy included in the analysis were defined as follows. All women who smoked at least one cigarette per day were defined as smokers. Smoking habits of the women and their partners were recorded based on interview responses. First trimester vaginal bleeding (FTBL) was defined as bleeding during the first 12 gestational weeks of pregnancy. Birth before 37 completed gestational weeks was defined as preterm. Chronic hypertension was defined as blood pressure ≥140/90mmHg before pregnancy or before the 20th week of gestation. Pregnancy-induced hypertension (PIH) was diagnosed if systolic blood pressure had increased by more than 30mmHg or diastolic blood

pressure by more than 15mmHg after the 20th gestational week exceeding 140/90mmHg, in the absence of proteinuria (<0.3g/l). Preeclampsia was defined as PIH with proteinuria (≥0.3g/l).

Data Management and Analysis

Data Entry

Data entry was done using SPPS-13 software. After recoding and cleaning procedures through sorting and spot checking, the data was transferred into STATA-10 statistical package for statistical analysis.

Statistical Methods

Basic descriptive statistics (means, frequencies, standard deviations, and confidence intervals) were generated for controls, cases and those whose case status was not confirmed during telephone interview (reclassified cases). The study used an independent t-test for comparison of means for continuous data and the Pearson's chi-square test to compare differences in proportions/means of independent variables between groups. Continuous variables were converted into ordinal variables to describe their distribution among cases and controls and to explore their relationships with the outcome variable. Categorical data were converted into "dummy" or binomial variables for the regression analysis.

To assess the relationships between outcome and each independent variable we performed simple logistic regression. Then the statistically significant risk factors were adjusted for multiple comparisons using the Bonferroni method. Study applied multiple logistic regression models to control for potential confounders and reveal potential effect modification. We calculated the odds ratios and 95% confidence intervals to estimate the strength of associations between outcome and independent variables.

Finally, the degree of collinearity among different risk factors in the final model was checked using variance inflation factor (VIF) method.

Ethical Considerations

The Institutional Review Board (IRB) within the College of Health Sciences at the American University of Armenia (AUA CHSR) reviewed and approved the study. All possible ethical issues of privacy and confidentiality have been taken into account while conducting the study. Oral consent was obtained from all participants before telephone interview (Appendix 3). Participants could skip any of the questions and stop the interview at any time. Personal information about the participants was available only to the researchers and was not used for other purposes. All participants were provided with AUA CHSR telephone numbers in case of complaints or other questions.

RESULTS

Response Rate

Overall, 385 record revisions were done and as a result163 potential cases and 222 controls were selected. Because of non-responding or changed contact information (56 cases and 50 controls) and 8 refusals (2 case and 6 controls), 271 complete telephone interviews were done. The response rate was 97.6% among cases and 96.5% among controls. The study team failed to contact subjects due to different reasons: being out of the country, not at home, wrong telephone numbers or the change of the telephone number.

As a result of telephone interviews we identified 83 cases (deliveries with placental abruption), 166 controls (deliveries without placental abruption), and 22 cases (all of them

delivered by Cesarean Section) whose “case” status was not confirmed by telephone interview (Table 2).

Descriptive Statistics

Descriptive statistical analysis by maternities was done to explore differences between participants from different facilities. No major differences were found regarding age, weight before pregnancy, weight at delivery or pregnancy termination, weight gain, height, BMI, gestational age at enrollment to antenatal care (ANC) in women consultation, number of ANC visits, blood loss, gestational age at delivery of pregnancy termination, number of pregnancies, age at menarche, age at sexual life initiation, weight of newborn, and interpregnancy intervals (Table 3). Regarding education and socioeconomic condition of family during pregnancy, analysis revealed differences among participants from different facilities (Table 4 and 5).

Initial analysis was conducted to compare “reclassified cases” with “cases” and “controls”. Results of this analysis showed that by the majority of variables “reclassified cases” do not differ from controls (Table 6). By the main statistically significant risk factors of placental abruption “reclassified cases” were in between of cases and controls. Based on information from medical records with further confirmation during telephone interviews, 6.63% of controls, 13.64% of “reclassified cases”, and 20.48% of cases ($p=0.005$) suffered from preeclampsia. First trimester bleeding that lasted three and more days was reported by 5.42% of controls, 13.64% of “reclassified cases”, and 19.28% of cases ($p=0.003$). Regular use of progestogen drug “Dufaston” in the first half of pregnancy was mentioned by 28.92%, 40.91%, and 50.60% ($p=0.003$) of controls, “reclassified cases”, and cases respectively. Tables 7 and 8 present differences in the levels of education and socioeconomic conditions among participants with different outcomes.

Taking into account the fact that “reclassified cases” mediate between “true” cases and controls, we decided to drop “reclassified cases” and continue analysis on 83 cases and 166 controls.

Table 9 presents descriptive statistics of the study population by cases and controls. The mean age of women at delivery in cases and controls was 26.7 (SD 4.6) and 26.4 (SD 4.8) years respectively. No statistically significant differences were found between cases and controls regarding the following variables: weight (kg) before pregnancy 57.4 (SD 9.6) vs. 57.3 (SD 9.2); weight at delivery or pregnancy termination 71.7 (SD 10.4) vs. 73.2 (SD 9.9); height (m) 1.61 (SD 0.06) vs. 1.62 (SD 0.06); BMI 22.1 (SD 3.3) vs. 21.9 (SD 3.3); gestational age (weeks) at enrollment to antenatal care 13 (SD 5.4) vs. 12.1 (SD 4.3).

We had only one case with diabetes mellitus whose placental abruption occurred after direct abdominal trauma, and one case with PlAb at previous pregnancy.

Cases and controls were statistically significantly different with respect to the highest level of education, weight gain during pregnancy, gestational age at pregnancy termination, bleeding in the first trimester (≥3 days), preeclampsia, “Dufaston” use during pregnancy, and sleeping position (Table 9).

Simple Logistic Regression

The results of simple logistic regression analysis for unadjusted association between placental abruption status and independent variables with crude odds ratios (OR), 95% confidence intervals (95% CI), and p-values are presented in Table 10. The crude OR of the association between first trimester vaginal bleeding and placental abruption was 4.2 (95%CI [1.8 – 9.9]; p=0.001) which means that women with three and more days of vaginal bleeding in the first trimester of pregnancy have 4.2 times higher risk of placental abruption. We decided to

consider three and more days of FTBL based on the shape of the lowess curve. Regarding association between weight gains during pregnancy and placental abruption status, we found that those women whose weight increased by less than 13 kg during pregnancy have twice the higher risk of placental abruption, compared to those with larger weight gain, and this difference was statistically significant (OR 2.1; 95% CI [1.2 - 3.7]; p=0.011). Women with less than four antenatal visits have almost 9 times higher risk for placental abruption compared to women with four and more visits to women's consultation (OR 8.8; 95%CI [1.8 - 42.2]; p=0.007). Among other significant risk factors were: preeclampsia (OR 3.6; 95%CI [1.6 - 8.2]; p=0.002), higher level (≥13 years) of education (OR 1.7; 95%CI [1.0 - 2.9]; p=0.049), sleeping on back position (OR 1.22; 95%CI [1.04 - 1.42]; p=0.014), and "Dufaston" use in the first half of the index pregnancy (OR 2.5; 95%CI [1.5 - 4.3]; p=0.001).

We did not find statistically significant differences between cases and controls with regards to risk factors mentioned in other studies: maternal age (OR 1.0; 95%CI [0.9 - 1.1]; p=0.674), women's blood groups (OR 0.9; 95%CI [0.6 - 1.2]; p=0.364), Rhesus factor (OR 2.1; 95%CI [0.9 - 4.7]; p=0.086), BMI (OR 1.0; 95%CI [0.9 - 1.1]; p= 0.706), Cesarean Section at the previous delivery (OR 1.4; 95%CI [0.6 - 3.5]; p=0.432), child's male sex (OR 1.2; 95%CI [0.7 - 2.1]; p=0.419). We have only 2 women in our sample who reported being smokers during index pregnancies and both of them were in the control group. Data analysis showed no association between exposure to second hand smoke and placental abruption (OR 1.02; 95%CI [0.93 - 1.12]; p=0.672).

After adjusting for multiple comparisons using the Bonferroni method "weight gain during pregnancy", "sleeping on back position", "higher level of education" no longer achieved statistical significance, while "first trimester vaginal bleeding", "preeclampsia", "Dufaston use

during pregnancy", and "number of ANC visits" (adjusted p=0.007) remained statistically significant. This suggests that even after accounting for the number of risk factors studied, first trimester vaginal bleeding helps predict placental abruption.

Testing for Confounders

Table 11 presents the results of simple logistic regression for the association between independent variables and placental abruption and first trimester vaginal bleeding and other independent variables. No statistically significant associations were found between FTBL and preeclampsia status (OR 0.7; p=0.591), sleeping on back position (OR 1.0; p=0.679), level of education with cut-off level of 13 years (OR 1.2; p=0.657), and weight gain during pregnancy with cut-off level of 13 kg (OR 1.4; p=0.441). Analysis revealed statistically significant association only between "Dufaston" use during pregnancy and first trimester vaginal bleeding (FTBL) (OR 11.8; p<0.001). "Dufaston" was found to be a confounder for the association between PlAb and FTBL, because it was strongly associated with both placental abruption and first trimester vaginal bleeding.

Multiple Logistic Regression

In the multiple logistic regression model, we included all statistically significant factors and also added the age, BMI, education and socioeconomic status. Table 12 presents crude and adjusted ORs and p-values of multivariate logistical regression. After adjusting for confounders, the odds of developing placental abruption was more than three times higher among women with the first trimester vaginal bleeding (OR 3.6; p=0.01) compared to women without FTBL. The odds of developing placental abruption was more than four times higher among women with preeclampsia (OR 4.6; p=0.001).

An interaction between preeclampsia and maternal age was detected. While there was no association between maternal age and placental abruption among women with normal blood pressure, in case of having preeclampsia every year increase in age was associated with 20 % increase in the risk of placental abruption.

After adjusting for confounders the statistical significance of "Dufaston" use on placental abruption became marginal (OR 1.8; p=0.057). Women with less than 13 kg weight gain during pregnancy have twice higher risk of developing PlAb compared with those who gained 13 kg and more (OR 2.2; p=0.014). The cut-off level of 13kg was decided based on changes of natural distribution of weight gain during pregnancy against the probability of being a case on the lowess curve. Compared with women with 13 and less year of education, women with higher education (>13 years) have twice higher odds of PlAb (OR 2.1; p=0.018). Sleeping on back position increases the risk of PlAb by 20% (OR 1.2; p=0.021).

Finally, we checked collinearity between statistically significant risk factors of placental abruption. The mean variance inflation factor (VIF) among risk factors of PlAb was 1.26, which allows stating that collinearity was not an issue in our model.

DISCUSSION

Main Findings

Women with three and more days of the first trimester vaginal bleeding during pregnancy had higher odds of placental abruption when compared with women without or less than three days of the FTBL. To the best of our knowledge, this is the first study examining associations between first trimester vaginal bleeding with placental abruption in Armenia.

Our findings are consistent with other studies reporting associations between FTBL, preeclampsia, sleeping position, and insufficient weight gain with PlAb(11;13;21;26;27;30;31). With regard to other risk factors for PlAb revealed in other studies, such as smoking, male sex of the fetus, Cesarean delivery in the previous birth, our study did not find statistically significant associations(4;24;30;32-35).

During data collection we paid attention to the high rates of Cesarean Section in all three facilities. Comparative analysis of modes of delivery for the last three years showed gradual and steady increase in rates of Cesarean Sections in Armenia on the whole and in Yerevan in particular: 22%, 25%, and 27% in 2008, 2009, and 2010 respectively(36). After "Obstetric Care Certificate"(37) introduction in Armenia on July 1, 2008 which provides differentiated reimbursement for childbirth depending on the level of maternal care facility and the mode of delivery (vaginal birth or cesarean section), there is a strong financial incentive for both obstetricians-gynecologists and maternal facilities to increase the rate of Cesarean Sections. Reimbursement for cesarean section is twice higher than for vaginal birth for hospitals and up to ten times higher for obstetrician-gynecologists. Placental abruption, being a diagnosis which in majority of cases requires quick and thus mainly operative delivery, sometimes might be used by obstetricians-gynecologists for justification of performed Cesarean Section. This might be a reasonable explanation for baffling high rate of PlAb and "reclassified cases" in one of the selected maternities.

Unlike other studies we did not find statistically significant association between maternal age and placental abruption. However an interesting interaction between preeclampsia and maternal age on placental abruption status was detected. Graphs 1 and 2 show the difference in associations between maternal age and placental abruption based on results of stratification by

preeclampsia status. In the case of preeclampsia, one year increase in age on average increases the risk of placental abruption by 20%.

A lot of studies have reported statistically significant association between maternal smoking and PlAb(13;14;16;32-34;38). However, our study failed to find any association either with maternal smoking or with second hand smoking. We have only two smokers in our sample, and both of them were in the control group.

Many studies reported statistically significant association between placental abruption and Cesarean delivery at previous pregnancy(6;24;38) and the majority of the reported cases occurred at term pregnancies (after 37 weeks of pregnancy). One possible explanation of why we did not find statistically significant association between PlAb and CS at previous pregnancy is that all women with previous CS are delivered by CS regardless of interpregnancy or interbirth intervals. Rate of vaginal birth after Cesarean Section (VBAC) in Armenia is approaching zero with few extremely rare exceptions. Women with previous CS undergo a planned CS if they have completed 38 gestational weeks, which prevents the majority of cases of PlAb later in pregnancy. This might be a possible explanation; however, it is only a hypothesis and needs confirmation. Early CS can be a factor which decreases also the association between PlAb and preeclampsia, because women with severe preeclampsia usually undergo CS much earlier.

Our study found strong association between “Dufaston” use and placental abruption. The most common conditions for “Dufaston” administration during pregnancy are the increased uterine tonicity and first trimester vaginal bleeding which are the signs of threatening abortion. The meta-analysis of fifteen trials with 2118 participants showed no statistically significant difference in the risk of spontaneous abortion between progestogens and placebo or no treatment groups(39). However, obstetrician-gynecologists continue to widely prescribe progestogens.

When we adjusted the association between "Dufaston" use and PlAb by FTBL, the OR decreased from 2.5 (p=0.001) to 2.0 (p=0.017). Further we included "Dufaston" use variable in a multivariate logistical regression model and adjusted for clinically sound confounders. As a result of regression, the association between "Dufaston" use during pregnancy and PlAb lost its statistical significance (OR 1.8; p=0.057). Our study revealed that "Dufaston" is a confounder of the association between PlAb and FTBL, because it was strongly associated with both placental abruption and first trimester vaginal bleeding. Application of variance inflation method did not reveal collinearity between "Dufaston" and FTBL.

Study Limitations

Several potential limitations should be considered when interpreting our results.

Selection bias:

Maternities were selected by convenience and only those facilities were included in the study whose administration agreed to provide delivery medical records of 2010 for record revision. However, the fact that almost forty percents of Yerevan deliveries in 2010 occurred in selected three maternities and that all available cases of placental abruption were included in analysis decreases the threats to external validity. Another possible source of selection bias was a poor quality of medical records' completion by doctors with absent or incorrect contact information. Thus, only women with correct contact information were interviewed and included in the analysis.

Recall bias:

Recall bias, which is peculiar to all retrospective studies, might be an issue in our study as well, particularly on drugs used during pregnancy. To minimize the recall bias we tried to collect as much information from medical records as possible and included in the analysis drugs about which participants were confident.

Lastly, although we adjusted for multiple confounding factors, we cannot exclude the possibility of some residual confounding.

Strength of the Study

This was a first attempt to investigate risk factors for placental abruption in Armenia. Diagnosis of placental abruption was confirmed during telephone interview. We conducted comparative analysis of "misclassified cases" with cases and controls to decide on those final statuses. Twenty two cases with placental abruption in the final diagnosis at the moment of pregnancy termination were considered reclassified, because their "case" status was not confirmed during telephone interviews. Our approach was the following: if there is no difference between mentioned 22 "reclassified cases" and other controls with Cesarean Section we will add them to the controls, otherwise we will exclude them from analysis. However, the results of preliminary analysis showed that by many important clinical factors "reclassified cases" are mediate between cases and control. Taking into account that even without "reclassified cases" we had sufficient number of participants we decided to continue analysis only based on "real" cases and controls.

To avoid interviewer bias, all interviews were conducted by the same person after pretesting and under the periodic supervision of student investigator. Interviewer was not aware of case-control status of interviewees.

The study used incidence density approach for selecting controls meaning that controls were selected from all eligible women that gave birth in the selected maternity homes without PlAb in diagnosis in the same time period when the cases were diagnosed with PlAb in the same maternity homes.

RECOMMENDATION

Further research is needed to replicate the findings of our study in Armenian population, especially on interaction between maternal age and preeclampsia on PlAb.

Our study did not measure the association between maternal stress and placental abruption, though some studies noted that the odds of PA increased with increasing severity of depressive symptoms(40). There is an opinion that stimulation of sympathetic nervous system and resultant hypertension, experienced during a panic attack or severe stress, might be the real factor causing PlAb(41). We would like to recommend include questions about stress and psychological disorders during pregnancy into a study instrument of future studies investigating risk factors for placental abruption.

Considering more risk factors in the next studies will give a chance to develop a predictive model for PlAb.

CONCLUSION

Overall the results of this investigation were consistent with previous studies. Our case-control study has demonstrated that first-trimester vaginal bleeding is an independent risk factor for placental abruption, and patients who reported three and more days of the first trimester vaginal bleeding showed an increased risk of placental abruption. A new finding which was an interaction between maternal age and preeclampsia status on placental abruption needs to be investigated and replicated in further studies.

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TABLES

Table 1. Numbers and Percentages of Cesarean Sections (CS) and Placental Abruptions (PlAb) in Selected Maternities in 2010

Maternity	N of births	N of CS	% of CS	N of PlAb	% of PlAb
"GN"MC	959	236	24.61	13	1.36
RCMCHP	3061	731	23.88	49	1.60
IPOG	3841	1332	34.68	279	7.26
Total	7861	2299	29.24	341	4.34

Table 2. Distribution of Participants by Maternity and Status

Maternity	Total	Non-respondent	Refusal	Complete	Cases	Controls	Reclassified
"GN"MC	45	8	3	34 (12.55%)	11	21	2 (15.4%)
RCMCHP	147	33	2	112 (41.33%)	28	80	4 (12.5%)
IPOG	193	65	3 (2 cases)	125 (46.12%)	44	65	16 (26.7%)
Total	385	106	8	271 (100%)	83	166	22 (21.0%)

Table 3. Descriptive Statistics by Maternities

Variable	Mean	Std. Dev	Min	Max
Age at delivery (year)				
"GN"MC (n=34)	25.59	4.64	18	36
RCMCHP (n=112)	26.53	4.84	18	38
IPOG (n=125)	26.7	4.73	16	40
Weight before pregnancy (kg)				
"GN"MC (n=34)	56.88	8.27	41	76
RCMCHP (n=112)	58.6	10.2	44	95
IPOG (n=125)	56.62	9.38	38	80
Weight at pregnancy termination (kg)				
"GN"MC (n=34)	71.44	7.04	54	86
RCMCHP (n=112)	73.55	11.12	51	111
IPOG (n=125)	72.49	10.86	50	105
Weight gain during pregnancy (kg)				
"GN"MC (n=34)	14.56	5.62	5	26
RCMCHP (n=112)	14.95	5.87	3	29
IPOG (n=125)	15.87	5.12	5	30
Height of woman (m)				
"GN"MC (n=34)	1.61	0.046	1.53	1.70
RCMCHP (n=112)	1.62	0.057	1.48	1.78
IPOG (n=125)	1.61	0.063	1.45	1.79
BMI (body mass index)				
"GN"MC (n=34)	21.93	3.48	16.85	32.47
RCMCHP (n=112)	22.33	3.62	17.31	36.20
IPOG (n=125)	21.8	3.25	15.82	33.30
GA at enrollment to ANC (weeks)				
"GN"MC (n=34)	14.5	7.2	5	33
RCMCHP (n=112)	12.2	4.5	5	32
IPOG (n=125)	11.9	3.5	3	24
Number of ANC visits				
"GN"MC (n=34)	6.1	2.35	0	12
RCMCHP (n=112)	6.2	1.67	2	12
IPOG (n=125)	6.6	2	3	14
Blood loss (ml)				
"GN"MC (n=34)	382	254	150	1000
RCMCHP (n=112)	425	231	250	1500
IPOG (n=125)	474	260	100	1500
GA at pregnancy termination (weeks)				
"GN"MC (n=34)	37.8	3.1	28	40
RCMCHP (n=112)	37.9	3.2	23	41
IPOG (n=125)	38.1	2.36	27	41
Number of pregnancies				
"GN"MC (n=34)	2.3	1.57	1	8
RCMCHP (n=112)	2.6	2.15	1	14
IPOG (n=125)	2.1	1.42	1	6

Menarche (y/o)				
“GN”MC (n=34)	13.5	1.16	11	16
RCMCHP (n=112)	13.7	1.32	12	20
IPOG (n=125)	13.3	1.2	9	18
Sexual life initiation (y/o)				
“GN”MC (n=34)	21.7	4.03	16	35
RCMCHP (n=112)	22	3.25	16	34
IPOG (n=125)	22.7	4.11	15	38
Child’s weight (g)				
“GN”MC (n=34)	2909.4	746.6	1000	4400
RCMCHP (n=112)	3005.2	689.9	500	4150
IPOG (n=125)	2995.3	594.4	1180	4100
Interpregnancy interval (years)				
“GN”MC (n=22)	1.98	1.6	0.5	6
RCMCHP (n=68)	2.25	1.9	0.4	11
IPOG (n=66)	2.49	2.3	0.5	13

Table 4. Differences in the Levels of Education Among Participants by Maternities

Education (year)	Maternity		
	"GN"MC	RCMCHP	IPOG
≤13	27 (79.41%)	49 (43.75%)	64 (51.20%)
≥13	7 (20.59%)	63 (56.25%)	61 (48.80%)
Total	34	112	125

Table 5. Differences in Socioeconomic Conditions (SEC) Among Participants from Different Maternities

SEC	Maternity		
	"GN"MC	RCMCHP	IPOG
Below average	3 (8.82%)	10 (8.93%)	11 (8.80%)
Average	12 (35.29%)	48 (42.86%)	63 (50.40%)
Above average	19 (55.88%)	54 (48.21%)	51 (40.80%)
Total	34	112	125

Table 6. Descriptive Statistics by Status

Variable	Mean	Std. Dev	Min	Max
Age at delivery (years)				
Controls (n=166)	26.41	4.75	18	40
Cases (n=83)	26.67	4.61	18	38
Reclassified cases (n=22)	26.36	5.57	16	38
Weight before pregnancy (kg)				
Controls (n=166)	57.25	9.18	38	95
Cases (n=83)	57.42	9.56	40	93
Reclassified cases (n=22)	59.36	12.97	44	95
Weight at pregnancy termination (kg)				
Controls (n=166)	73.16	9.89	50	107
Cases (n=83)	71.7	10.38	54	100
Reclassified cases (n=22)	74.18	15.43	51	111
Weight gain during pregnancy (kg)				
Controls (n=166)	15.91	5.54	3	29
Cases (n=83)	14.28	5.42	5	30
Reclassified cases (n=22)	14.82	5.17	7	25
Height of woman (m)				
Controls (n=166)	1.62	0.06	1.46	1.79
Cases (n=83)	1.61	0.06	1.45	1.74
Reclassified cases (n=22)	1.6	0.06	1.5	1.72
BMI (body mass index)				
Controls (n=166)	21.9	3.34	15.8	36.2
Cases (n=83)	22.1	3.33	16	35.4
Reclassified cases (n=22)	23	4.41	17.6	33.3
GA at enrollment to ANC (weeks)				
Controls (n=166)	12.1	4.3	5	32
Cases (n=83)	13	5.4	3	33
Reclassified cases (n=22)	12.2	3.3	6	19
Number of ANC visits				
Controls (n=166)	6.6	1.8	2	14
Cases (n=83)	5.8	2.1	0	14
Reclassified cases (n=22)	6.2	1.5	4	10
Blood loss (ml)				
Controls (n=166)	299	137	100	850
Cases (n=83)	686	228	200	1500
Reclassified cases (n=22)	606	132	200	800
GA at pregnancy termination (weeks)				
Controls (n=166)	38.8	1.75	24	41
Cases (n=83)	36.3	3.65	23	41
Reclassified cases (n=22)	38.1	2.57	29	40
Number of pregnancies				
Controls (n=166)	2.3	1.8	1	14
Cases (n=83)	2.4	1.9	1	8
Reclassified cases (n=22)	2.1	1.5	1	6

Variable	Mean	Std. Dev	Min	Max
Menarche (y/o)				
Controls (n=166)	13.6	1.3	10	20
Cases (n=83)	13.4	1.1	11	18
Reclassified cases (n=22)	12.8	1.2	9	14
Sexual life initiation (y/o)				
Controls (n=166)	22.3	3.4	17	36
Cases (n=83)	22.4	4.3	16	38
Reclassified cases (n=22)	22	4.4	15	31
Child's weight (g)				
Controls (n=166)	3170	492	700	4400
Cases (n=83)	2599	784	500	4070
Reclassified cases (n=22)	3086	563	1370	3900
Interpregnancy interval (years)				
Controls (n=99)	2.3	2	0.5	13
Cases (n=46)	2.1	2.1	0.4	11
Reclassified cases (n=11)	2.9	2.2	1	7

Table 7. Differences in the Levels of Education Among Participants by Status

Education (year)	Status		
	Control	Case	Reclassified case
≤13	94 (56.63%)	36 (43.37%)	10 (45.45%)
≥13	72 (43.37%)	47 (56.63%)	12 (54.55%)
Total	166	83	22

Table 8. Differences in Socioeconomic Conditions (SEC) Among Participants by Status

SEC	Status		
	Control	Case	Reclassified case
Below average	14 (8.43%)	9 (10.84%)	1 (4.55%)
Average	76 (45.78%)	36 (43.37%)	11 (50.00%)
Above average	76 (45.78%)	38 (45.78%)	10 (45.45%)
Total	166	83	22

Table 9. Descriptive Statistics by Cases and Controls

Variable		Status		p – value
		Controls 66.7% (n=166)	Cases 33.3% (n=83)	
Age at delivery (years)				
	Mean	26.4	26.7	
	SD	4.8	4.6	0.675
	CI	25.7 – 27.1	25.7 – 27.7	
Weight before pregnancy (kg)				
	Mean	57.3	57.4	
	SD	9.2	9.6	0.895
	CI	55.8 – 58.6	55.3 – 59.5	
Weight at pregnancy termination (kg)				
	Mean	73.2	71.7	
	SD	9.9	10.4	0.280
	CI	71.6 – 74.7	69.4 – 74	
Weight gain during pregnancy (kg)				
	Mean	15.9	14.3	
	SD	5.5	5.4	0.029
	CI	15 – 16.8	13 – 15.5	
Height of woman (m)				
	Mean	1.62	1.61	
	SD	0.06	0.06	0.552
	CI	1.61 – 1.62	1.6 – 1.62	
BMI (body mass index)				
	Mean	21.9	22.1	
	SD	3.3	3.3	0.707
	CI	21.4 – 22.4	21.3 – 22.8	
GA at enrollment to ANC (weeks)				
	Mean	12.1	13	
	SD	4.3	5.4	0.124
	CI	11.4 – 12.7	11.8 – 14.2	
Number of ANC visits				
	Mean	6.6	5.8	
	SD	1.8	2.1	<0.01
	CI	6.4 – 6.9	5.4 – 6.3	
Blood loss (ml)				
	Mean	299	686	
	SD	137	228	<0.01
	CI	278 - 320	637 - 736	
GA at pregnancy termination (weeks)				
	Mean	38.8	36.3	
	SD	1.8	3.6	<0.01
	CI	38.6 – 39.1	35.5 - 37	
Number of pregnancies				

Variable		Status				p – value
		Controls 66.7% (n=166)		Cases 33.3% (n=83)		
	Mean	2.3		2.4		
	SD	1.8		1.9		0.586
	CI	2 – 2.6		2 – 2.8		
Interpregnancy interval (years)		(n=99)		(n=46)		
	Mean	1.4		1.2		
	SD	1.9		1.9		0.401
	CI	1.1 – 1.7		0.8 – 1.6		
Menarche (y/o)						
	Mean	13.6		13.4		
	SD	1.3		1.1		0.235
	CI	13.4 – 13.8		13.2 – 13.7		
Sexual life initiation (y/o)						
	Mean	22.3		22.4		
	SD	3.4		4.3		0.867
	CI	21.7 – 22.8		21.4 – 23.3		
Child's weight (g)						
	Mean	3170		2600		
	SD	492		784		<0.01
	CI	3095 - 3246		2428 - 2771		
Working hours						
	Mean	2		2.4		
	SD	3.1		3.4		0.398
	CI	1.6 – 2.5		1.6 – 3.2		
Secondhand smoking (hours)						
	Mean	1.8		2		
	SD	2.7		3.1		0.673
	CI	1.4 – 2.2		1.3 – 2.6		
Blood groups						
	I(O)	44	26.51%	25	30.12%	
	II(A)	81	48.80%	41	49.40%	
	III(B)	29	17.47%	13	15.66%	0.832
	IV(AB)	12	7.23%	4	4.82%	
Rhesus factor						
	No	30	18.07%	8	9.64%	0.081
	Yes	136	81.93%	75	90.36%	
Preeclampsia						
	No	155	93.37%	66	79.52%	<0.01
	Yes	11	6.63%	17	20.48%	
Mode of delivery						
	Vaginal birth	131	78.92%	7	8.43%	<0.01
	Cesarean Section	35	21.08%	76	91.57%	

Variable		Status				p – value
		Controls 66.7% (n=166)		Cases 33.3% (n=83)		
CS at previous delivery						
	No	153	92.17%	74	89.16%	0.430
	Yes	13	7.83%	9	10.84%	
Sex of newborn						
	Female	81	48.80%	36	43.37%	0.419
	Male	85	51.20%	47	56.63%	
Employment during pregnancy						
	No	108	65.06%	53	63.86%	
	Yes	57	34.34%	29	34.94%	0.874
	Student	1	0.6%	1	1.2%	
Physically hard work						
	No	148	89.16%	73	87.95%	0.777
	Yes	18	10.84%	10	12.05%	
Contact with chemicals						
	No	162	97.59%	80	96.39%	0.588
	Yes	4	2.41%	3	3.61%	
Sleeping on back position						
	No	140	84.34%	58	69.88%	
	Yes	24	14.46%	19	22.89%	<0.01
	Do not know	2	1.2%	6	7.23%	
Bleeding in the first trimester						
	No	132	79.52%	57	68.67%	0.059
	Yes	34	20.48%	26	31.33%	
Bleeding in the first trimester (≥3 days)						
	No	157	94.58%	67	80.72%	<0.01
	Yes	9	5.42%	16	19.28%	
Regular sex during pregnancy (≥1/week)						
	No	76	45.78%	50	60.24%	
	Yes	87	52.41%	33	39.76%	0.06
	Refused to respond	3	1.81%	0	0.00%	
Low BMI (<18.5)						
	No	149	89.76%	74	89.16%	0.883
	Yes	17	10.24%	9	10.84%	
Preterm deliveries						
	No	158	95.18%	51	61.45%	<0.01
	Yes	8	4.82%	32	38.55%	
Parity						
	Primipara	67	40.36%	37	44.58%	0.525
	Multipara	99	59.64%	46	55.42%	
Marital status (married)						
	No	6	3.61%	7	8.43%	0.107
	Yes	160	96.39%	76	91.57%	

Variable	Status				p – value
	Controls 66.7% (n=166)		Cases 33.3% (n=83)		
Socioeconomic condition of family					
Below average	14	8.43%	9	10.84%	0.811
Average	76	45.78%	36	43.37%	
Above average	76	45.78%	38	45.78%	
Level of education (years)					
≤13 years	94	56.63%	36	43.37%	0.048
>13 years	72	43.37%	47	56.63%	
Dufaston use during pregnancy					
No	118	71.08%	41	49.40%	<0.01
Yes	48	28.92%	42	50.60%	

Table 10. Statistically Significant Crude ORs of Associations Between Risk Factors and Placental Abruption

Variable		OR	95% CI		p – value
Weight gain during pregnancy (kg)		0.95	0.9	0.99	0.03
	≥13kg	1.00			
	<13kg	2.08	1.18	3.66	0.011
Number of ANC visits		0.8	0.68	0.93	0.004
	≥4 visits	1.00			
	<4 visits	8.75	1.81	42.2	0.007
Preeclampsia					
	No	1.00			
	Yes	3.63	1.6	8.2	0.002
Sleeping on back position					
	No	1.00			
	Yes	1.22	1.04	1.42	0.014
Bleeding in the first trimester (≥3 days)					
	No	1.00			
	Yes	4.2	1.8	9.9	0.001
Dufaston use during pregnancy					
	No	1.00			
	Yes	2.52	1.46	4.34	0.001
Level of education					
	≤13 years	1.00			
	>13 years	1.7	1.0	2.9	0.049

Table 11. Testing For Confounding

Variable		Association between PlAb and covariates		Association between FTBL and covariates	
		OR	p - value	OR	p – value
Preeclampsia					
	No	1.00		1.00	
	Yes	3.63	0.002	0.66	0.591
Dufaston use during pregnancy					
	No	1.00		1.00	
	Yes	2.52	0.001	11.8	<0.01
Sleeping on back position					
	No	1.00		1.00	
	Yes	1.22	0.014	1.04	0.679
Level of education					
	≤13 years	1.00		1.00	
	>13 years	1.7	0.049	1.2	0.657
Weight gain during pregnancy (kg)					
	≥13kg	1.00			
	<13kg	2.08	0.011	1.41	0.441

Table 12. Crude and Adjusted ORs After Controlling For Confounders

Variable	Crude		Adjusted	
	OR	**p - value**	**OR**	**p - value**
Bleeding in the first trimester (≥3 days)				
No	1.00		1.00	
Yes	4.2	0.001	3.55	0.010
Preeclampsia				
No	1.00		1.00	
Yes	3.63	0.002	4.58	0.001
Dufaston use during pregnancy				
No	1.00		1.00	
Yes	2.52	0.001	1.83	0.057
Sleeping on back position				
No	1.00		1.00	
Yes	1.22	0.014	1.2	0.021
Level of education				
≤13 years	1.00		1.00	
>13 years	1.7	0.049	2.1	0.018
Weight gain during pregnancy (kg)				
≥13kg	1.00		1.00	
<13kg	2.08	0.011	2.24	0.014

Table 12 shows the results of multivariate logistical regression for age, BMI, education, socioeconomic condition of family during pregnancy, first trimester bleeding, preeclampsia, "Dufaston" use, weight gain during pregnancy, and sleeping position.

FIGURES

Figure 1. Relationship Between Age and Placental Abruption for Women with Normal Blood Pressure

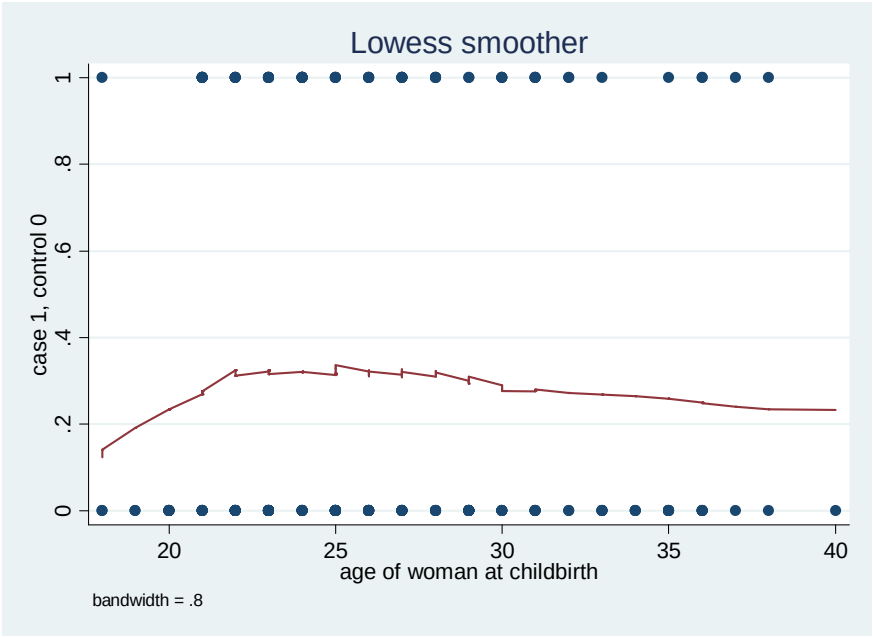
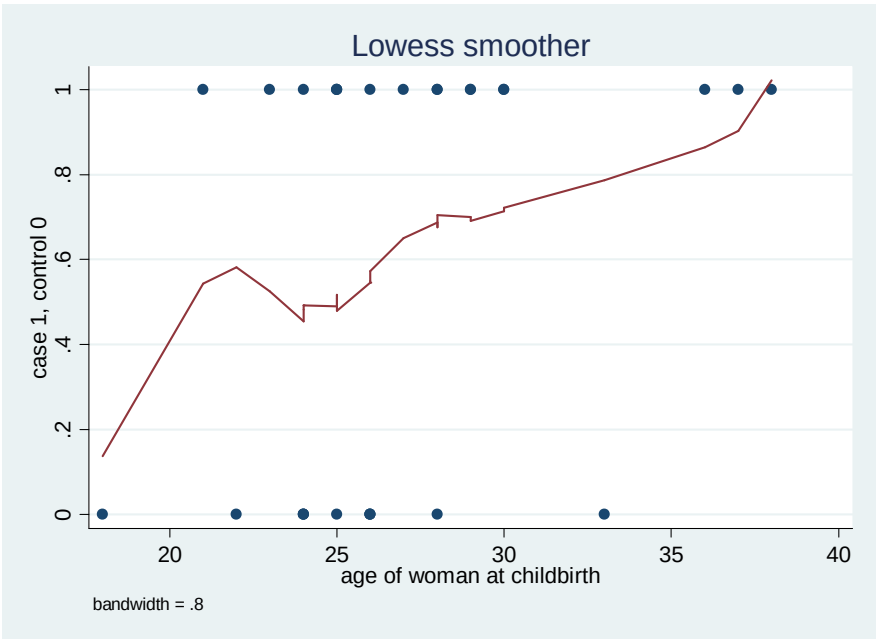


Figure 2. Relationship Between Age and Placental Abruption for Women with Preeclampsia



APPENDICES

Appendix 1 Record Review Form

1.	Name Surname, #of record form	
2.	Maternity home/obstetrical dept	
3.	Admission date, hosp. stay (days)	
4.	Date of birth (D/M/Y)	
5.	Marital status	
6.	Address/telephone	
7.	Diagnosis final	
8.	GA(weeks) at enrollment to ANC and N of visits	
9.	ABO Rh factor	
10.	Hb at admission g/l	
11.	Weight (kg) and Height (sm)	
12.	BP at admission (mmHg)	
13.	Blood loss (ml)	
14.	Ob/Gyn history (intervals, number) parity	
15.	LNM (D/M/Y)	
16.	Menarche (y/o)	
17.	Sex.life from y/o	
18.	Received treatment	
19.	Haemotransfusion: yes/no	
20.	Child status: Apgar scores, sex, weight (g)	

Appendix 2 Questionnaire

Risk factors for placental abruption: case-control study

QUESTIONNAIRE

ID_____ **Status:** 1. Case 0. Control

Date of the interview: _ _ _ _ /_ _ _ _ /_ _ _ _
(Day) (Month) (Year)

1.Maternity Hospital_____

2.Date of birth _ _ _ _/_ _ _ _/_ _ _ _
(Day) (Month) (Year)

3.Indicate the highest level of education that you have completed.

1. School (less than 10 years)
2. School (10 years)
3. Professional technical education (10-13 years)
4. Institute/University
5. Postgraduate

4.Have you been told by a physician that you had or have each condition below? *(Check **all** that apply)*

Hypertension	
Rheumatoid arthritis	
Renal disease	
Diabetes	
Endometritis	
Peptic ulcer	
Thyroid disease	

5.What was your marital status during that pregnancy?

1. single
2. married (booked or not)
3. divorced
4. widowed
5. refused to respond

6.How much did you weight before that pregnancy? _____kg 11. Don't know

7.How tall are you? _____cm 11. Don't know

8. How would you rate your family's general standard of living during that pregnancy?

1. Substantially below average
2. Little below average
3. Average
4. Little above average
5. Substantially above average
22. Refused to answer

9. Were you employed during that pregnancy?

1. Yes, *specify* _____
2. No (go to question 13)
3. I was a student

10. What were your working hours? _____ hours.

11. Did you perform a physically hard work during pregnancy either at home or in working place which required continuous muscle tension or forced position?

1. Yes, specify _____
2. No

12. Did you have regular contact with chemicals (including agro pesticides) during pregnancy?

1. Yes, specify _____
2. No

13. What sleeping position did you usually use during that pregnancy?

1. on the back
2. on the left side
3. on the right side
11. don't know

14. Did you smoke during that pregnancy?

1. Sometimes _____ cigarettes per week
2. Daily_____ cigarettes per day
3. I stopped smoking at ___ weeks of that pregnancy
4. No

15. Were there cigarette smokers living in your home or in workplace during that pregnancy?

1. Yes
2. No (go to question 17)

16. During that pregnancy, about how many hours a day, on average, were you in the same room with another person who was smoking? _____hours/day

17. Did you have bloody discharge in the first trimester of that pregnancy?

1. Yes
2. No (go to question 24)

18. How long the bloody discharge lasted?

1. It was one episode
2. 1 day
3. 2 days
4. 3 days
5. more than 3 days

19. Have you been hospitalized during that pregnancy?

1. Yes
2. No (go to question 23)

20. What was the main reason for hospitalization?

1. Threatened abortion (GA<22w)
2. Threatened premature delivery
3. Urinary tract infection
4. Hypertension (including chronic, gestational hypertensions, and preeclampsia)
5. Other, specify_____

21. Did you take any medications or vitamins during pregnancy?

1. Yes
2. No (go to question 24)
11. Do not remember

22. What drugs, suppositories, or injections did you receive?

Progesterone	
NSAID (aspirine, ibuprofen, analgin or other)	
Antimicrobial (antibiotics or other)	
Suppositories	
Other	

23. What was the reason for drug prescription?

Specify_____

24. Did you have high temperature (>38^{0}C) more than 1 day, or any other symptoms of infection during pregnancy?

1.Yes
2.No (go to question 26)
11. Do not remember (go to question 26)

25. What infections were diagnosed during that pregnancy?

Specify_____

26. Did you continue regular sexual life during that pregnancy?

1. Yes
2. No (go to question 30)
22. Refused to respond (go to question 30)

27. How often did you have intercourse during pregnancy?

1. Less than once a week
2. Once a week
3. More than once a week
22. Refused to respond

28. What was the reason for interruption?_____

29. *Ask only women who delivered with Cesarean Section*: In your opinion, what was the reason of Cesarean Section in your case?

_____
_____
_____
_____

Thank you for participation!

Ընկերքի շերտազատման ռիսկի գործոնները. դեպք-ստուգիչ հետազոտություն

Հարցաթերթիկ

ID_____

Կարգավիճակը: 1. դեպք 0. ստուգիչ

Հարցազրույցի ամսաթիվը _ _ _ _/_ _ _ _/_ _ _ _
(օր) (ամիս) (տարի)

1. **Ծննդատունը**_____

2. **Ծննդյան ամսաթիվ** _ _ _ _/_ _ _ _/_ _ _ _
(օր) (ամիս) (տարի)

3. **Նշեք ամենաբարձր կրթությունը, որ Դուք ստացել եք:**
   1. Թերի միջնակարգ (դպրոց, 10 տարուց պակաս)
   2. Միջնակարգ (դպրոց, 10 տարի)
   3. Միջին մասնագիտական (ուսումնարան, 10-13 տարի)
   4. Բարձրագույն (ինստիտուտ կամ համալսարան, 14 տարի)
   5. Հետդիպլոմային (մագիստրատուրա, ասպիրանտուրա, դոկտորանտուրա, >15 տարի)

4. **Ձեզ երբևէ բժիշկ ասե՞լ է, որ ունեք հետևյալ վիճակներից որևէ մեկը՝**
(Նշեք բոլոր համապատասխանող տարբերակները)

Բարձր ճնշում	
Ռևմատոիդ հոդաբորբ	
Երիկամային հիվանդություն	
Շաքարախտ	
էնդոմետրիտ	
12-մատնյա աղու խոց	
Վահանագեղձի հիվանդություն	

5. **Ձեր ամուսնական կարգավիճակը այդ հղիության ընթացքում**:
   1. Միայնակ
   2. Ամուսնացած (գրանցված է, թե ոչ)
   3. Ամուսնալուծված
   4. Այրի
   22. Հրաժարվում եմ պատասխանել

6. **Որքա՞ն էր Ձեր քաշը մինչ այդ հղիությունը** _____**կգ** 11. Չգիտեմ

7. **Որքա՞ն է Ձեր հասակը** _____**սմ** 11. Չգիտեմ

8. Ընդհանուր առմամբ, ինչպե՞ս կբնութագրեիք Ձեր ընտանիքի կենսամակարդակը այդ հղիության ընթացքում: *(Կարդացեք պատասխանները)*

1. Միջինից բավականին ցածր
2. Միջինից մի փոքր ցածր
3. Միջին
4. Միջինից մի փոքր բարձր
5. Միջինից բավականին բարձր
22. Հրաժարվում եմ պատասխանել

9. Դուք աշխատու՞մ էիք այդ հղիության ընթացքում:

1. Այո
2. Ոչ (Անցեք հարց 11)
3. Ես ուսանող էի

10. Միջինում օրական քանի՞ ժամ էիք աշխատում:_____ժամ

11. Այդ հղիության ընթացքում Դուք կատարե՞լ եք ֆիզիկական ծանր աշխատանք, որը պահանջում էր մկանային շարունակական լարվածություն կամ հարկադիր դիրք:

1. Այո, նշեք տեսակն ու տևողությունը_____
2. Ոչ

12. Այդ հղիության ընթացքում Դուք կանոնավոր շփում ունեցե՞լ եք քիմիականների (ներառյալ գյուղատնտեսական պարարտանյութերը) հետ:

1. Այո, նշեք տեսակն ու տևողությունը _____
2. Ոչ

13. Ի՞նչ դիրքով եք սովորաբար քնել այդ հղիության ընթացքում:

4. Մեջքի վրա
5. Ձախ կողքի վրա
6. Աջ կողքի վրա
11. Չգիտեմ

14. Դուք ծխու՞մ էիք այդ հղիության ընթացքում:

1. Երբեմն_____ գլանակ շաբաթական
2. Ամեն օր _____ գլանակ օրական
3. Դադարեցրել եմ այդ հղիության _____ շաբաթում
4. Ոչ

15. Այդ հղիության ընթացքում Ձեր տանը կամ աշխատանքի վայրում կայի՞ն ծխող մարդիք:

1. Այո
2. Ոչ (Անցեք հարց 17)

16. Այդ հղիության ընթացքում, օրական միջինում քանի ժամ էիք գտնվում միևնույն սենյակում, որտեղ տվյալ պահին կար ծխող անձ: _____ժամ

17. Այդ հղիության առաջին եռամսյակում Դուք ունեցե՞լ եք արյունային արտադրություն կամ արյունահոսություն:

1. Այո
2. Ոչ (Անցեք հարց 19)

18. Որքա՞ն է տևել արյունային արտադրությունը:

1. Ընդամենը մի դրվագ էր
2. 1 օր
3. 2 օր
4. 3 օր
5. ավելի քան 3 օր

19. Այդ հղիության ընթացքում Դուք հիվանդանոցում պառկե՞լ եք:

1. Այո
2. Ոչ (Անցեք հարց 21)

20. Ո՞րն էր հիվանդանոց պառկելու հիմնական պատճառը:

1. Սպառնացող վիժում (հղիության ժամկետը<22շաբաթից)
2. Սպառնացող վաղաժամ ծննդաբերություն
3. Միզուղիների վարակ
4. Բարձր զարկերակային ճնշում(ներառյալ խրոնիկ, հղիությամբ պայմանավորված հիպերտենզիան և պրեէկլամպսիա)
5. Այլ, նշեք_____

21. Այդ հղիության ընթացքում Դուք օգտագործե՞լ եք որևէ դեղորայք կամ վիտամիններ:

1. Այո
2. Ոչ (Անցեք հարց 24)
11. Չեմ հիշում

22. Ի՞նչ հաբեր, ներարկումներ, մոմիկներ եք ստացել այդ հղիության ընթացքում և քանի՞ օր:

Պրոգեստերոն (դյուֆաստոն, ուտրոժեստան)	
ՈՍՀԲԴ (ասպիրին, իբուպրոֆեն, անալգին կամ այլ)	
Հակամանրէային (հակաբիոտիկներ կամ այլ)	
Մոմիկներ	
Այլ	

23. Որո՞նք էին դեղորայքը նշանակելու պատճառները:

Պարզաբանեք_____

24. Այդ հղիության ընթացքում Դուք ունեցե՞լ եք մեկ օրից երկար տևողությամբ բարձր ջերմություն (>38^0C) կամ ինֆեկցիայի այլ նշան:

1. Այո
2. Ոչ (Անցեք հարց 26)
11. Չեմ հիշում (Անցեք հարց 26)

25. Ինչպիսի՞ վարակներ են ախտորոշվել այդ հղիության ընթացքում, ո՞ր ժամկետում և որքա՞ն են տևել:

Նշեք_____
_____

26. Այդ հղիության ընթացքում Դուք շարունակե՞լ եք կանոնավոր սեռական կյանքը:

1. Այո
2. Ոչ (Անցեք հարց 30)
22. Հրաժարվում եմ պատասխանել

27. Որքա՞ն հաճախ եք Դուք հարաբերություն ունեցել այդ հղիության ընթացքում:

1. Շաբաթը մեկ անգամից քիչ
2. Շաբաթը մեկ
3. Շաբաթը մեկ անգամից հաճախ
22. Հրաժարվում եմ պատասխանել

28. Ո՞րն էր սեռական կյանքն ընդհատելու պատճառը:_____

29. ***Հարցրեք միայն Կեսարյան հատումով ծննդալուծված կանանց:*** **Ըստ Ձեզ, Ձեր դեպքում ինչն էր Կեսարյան հատում կատարելու պատճառը:**

_____
_____
_____
_____

Շնորհակալություն մասնակցության համար:

Appendix 3 Consent Form

American University Of Armenia
Institutional Review Board # 1/Committee On Human Research
College Of Health Sciences Subcommittee For Student Theses

CONSENT FORM

Title of Research Project: Risk Factors for Placental Abruption: case-control study

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Hello, my name is Karen Adamyan. I am an obstetrician-gynecologist and a graduate student in the School of Public Health of the American University of Armenia. We are conducting a study to investigate the risk factors for placental abruption. The research is conducted among women who delivered a baby in 2010 with or without placental abruption.

You have been selected to participate in this study because you had childbirth in 2010. Your contact information has been obtained from your medical record from the maternity home where you gave childbirth.

If you are willing to participate I will ask you several questions regarding your health status, and reproductive history. The interview will last no more than 15 minutes.

Your participation in the study is voluntary. You may skip any question you think is inappropriate and even stop the interview at any moment you want without any undesirable consequences for you. Also you can ask any questions you may have about this research study.

Your participation in the study poses no risk for you. The information obtained from you will help us understand the risk factors for placental abruption. It will be your contribution to science. There is no monetary benefit for the participation in this interview.

The information you provided is fully confidential and will be used only for the study. Anonymity will be maintained, your name will not appear on questionnaire. Only general findings will be presented at the end of the research. Contact information will be destroyed upon completion of the research.

If you have more questions about this study you can contact Dr. Varduhi Petrosyan, the Associate Dean of the College of Health Sciences at AUA calling 512592.
If you feel you have not been treated fairly or think you have been hurt by joining this study, please contact Dr. Hripsime Martirosyan, AUA Human Subjects Administrator at 51 25 61.

If you consent to participate, we can start.

Հայաստանի ամերիկյան համալսարան
Գիտահետազոտական էթիկայի հանձնաժողով
Հանրային առողջապահության ֆակուլտետ
Բանավոր համաձայնագիր

Հետազոտության անվանումը՝

Ընկերքի շերտազատման ռիսկի գործոնները. դեպք ստուգիչ հետազոտություն

Բարև Ձեզ, ես Կարեն Ադամյանն եմ: Ես մանկաբարձ-գինեկոլոգ եմ և Հայաստանի ամերիկյան համալսարանի հանրային առողջապահության ֆակուլտետի ավարտական կուրսի ուսանող եմ: Մենք հետազոտություն ենք իրականացնում, որի նպատակն է բացահայտել ընկերքի շերտազատմանը նպաստող ռիսկի գործոնները: Հետազոտությունն իրականացվում է կանանց շրջանում, ովքեր ծննդաբերել են 2010 թ-ին ընկերքի շերտազատումով, կամ առանց: Դուք ընտրվել եք մասնակցելու այս հետազոտությանը քանի որ ծննդաբերել եք 2010 թ-ի ընթացքում: Ձեր տվյալները վերցվել են ծննդատան ծննդաբերության պատմության քարտից:

Եթե Դուք համաձայն եք մասնակցել այս հետազոտությանը, կխնդրեի պատասխանել Ձեր առողջական վիճակի և վերարտադրողական պատմության վերաբերյալ հարցերին: Հարցազրույցը կտևի ոչ ավելի, քան 15 րոպե:

Ձեր մասնակցությունը այս հետազոտությանը կամավոր է: Դուք իրավունք ունեք չպատասխանել այն հարցերին, որոնց հարմար չեք գտնում պատասխանել և նույնիսկ ցանկացած պահի դադարեցնել հարցազրույցը, ինչը Ձեզ վրա որևէ բացասական հետևանքներ չի ունենա: Դուք կարող եք հարցեր տալ հետազոտության վերաբերյալ:

Ձեր մասնակցությունը այս հետազոտությանը որևէ ռիսկ չի ներկայացնում Ձեզ համար: Ձեր կողմից տրամադրված տվյալները կօգնեն մեզ բացահայտելու ընկերքի շերտազատմանը նպաստող ռիսկի գործոնները: Դա կլինի Ձեր ավանդը գիտության մեջ: Այս հարցազրույցին Ձեր մասնակցությունը չի ենթադրում որևէ դրամական խրախուսանք:

Ձեր կողմից տրամադրված տվյալները գաղտնի են պահվելու և օգտագործվելու են միայն հետազոտության նպատակով: Անանունության սկզբունքը պահպանվելու է, Ձեր անունը չի երևալու հարցաթերթիկի վրա: Միայն ամփոփիչ ադրյունքներն են ներկայացվելու հետազոտության ավարտին: Ձեր հաղորդակցության տվյալները կոչնչացվեն հետազոտության ավարտից անմիջապես հետո:

Հետազոտության հետ կապված հետագա հարցերի համար Դուք կարող եք զանգահարել Հայաստանի ամերիկյան համալսարանի հանրային առողջապահության ֆակուլտետի փոխդեկան Վարդուհի Պետրոսյանին 51 25 64 հեռախոսահամարով: Եթե գտնում եք, որ ձեզ հետ անարդարացի են վարվել կամ մտածում եք, որ մասնակցությունը վնաս է հասցրել Ձեզ, Դուք կարող եք զանգահարել ՀԱՀ էթիկայի հանձնաժողովի ադմինիստրատոր Հռիփսիմե Մարտիրոսյանին 51 25 61 հեռախոսահամարով:

Եթե համաձայն եք, կարող ենք սկսել:

Appendix 4 The List of Independent Variables of the Study

#	**Variable**	**Definition**
1	id	interview id
2	mid	maternity id: 1-“GN”MC; 2-RCMCHP; 3-IPOG
3	bd	birth day of woman
4	age	age of woman at index childbirth
5	date	date of childbirth
6	abo	blood group
7	rh	Rhesus factor: positive 1, negative 0
8	weight_1	weight of woman before pregnancy (kg)
9	weight_2	weight of woman at pregnancy termination (kg)
10	weight_g	weight gain during pregnancy (kg)
11	height	height of woman (m)
12	bmi	body mass index
13	ga_anc	gestational age (weeks) at enrollment to ANC
14	n_visit	number of antenatal care (anc) visits
15	hyperten	hypertension: 1 yes, 0 no
16	blooss	blood loss (ml)
17	ga	gestational age (weeks)
18	mod	mode of delivery: 1 c-section, 0 vaginal birth
19	cs_prev	cesarean section at previous delivery: 1 yes, 0 no
20	pregn	number of pregnancies
21	pm	partus maturus (term delivery)
22	prem	partus prematurus (preterm delivery)
23	stbirth	number of stillbirths
24	spab	number of spontaneous abortions
25	artab	number of artificial abortions
26	ect	number of ectopic pregnancies
27	pregint	years between pregnancies
28	lnm	date of last normal menses
29	menarche	age at menarche
30	sexlife	age at sex initiation
31	haemotr	haemotransfusion: 1yes, 0 no
32	childsex	sex of newborn: 1 male, 0 female
33	childwei	weight of newborn (g)
34	educ	highest education
35	marst	marital status
36	sec	socioeconomic conditions of family during pregnancy
37	employ	employment status during pregnancy: 1 yes, 0 no, 2 student
38	work_hou	average working hours per day during pregnancy
39	hardwork	phisically hard work during pregnancy: yes 1, no 0
40	chemcont	contact with chemicals during pregnancy: yes 1, no 0
41	sl_pos	sleeping position during pregnancy: 1 back, 0 other

42	smok_st	number of cigarettes per day during pregnancy
43	shs	hours of exposure to second hand smoking during pregnancy
44	ftbl	first trimester bleeding: yes 1, no 0
45	ftbl_dur	duration of the first trimester bleeding (days)
46	dufaston	dufaston use during pregnancy
47	high_tem	duration of high temperature (above 38) days
48	rslp	regular sex during pregnancy
49	sev_plab	severe blood losss ($\geq$ 1000)
50	sev_bl	first trimester bleeding $\geq$ 3 days