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Predictors of Miscarriage in the West of Iran: A Case-Control Study

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Abstract

Background: Since the risk factors for miscarriage vary in different societies, the present study was conducted to investigate the effect of the related factors on miscarriage in the west of Iran (Zanjan city). We aimed to determine the modifiable and non-modifiable predictors of miscarriage.

Methods: In this case-control study, 219 cases and 420 controls were selected among those living in the Zanjan (a city located in western Iran) in 2019. Data were collected by a 25-item checklist of medical records available in the comprehensive urban health service center. For assessing the effects of explanatory variables on miscarriage, the multiple logistic regression model was used at a 95% confidence interval. All analysis was conducted by Stata 14 software.

Results: Short birth interval (less than 36 months) (OR=2.4, $p<0.001$) and ectopic pregnancy (OR=3.5, $p<0.011$) increase the odds of miscarriage. In other words, high education reduced the odds of miscarriage (OR:0.07,$p<0.001$).

Conclusion: In the present study, increasing age, low education level, history of previous coagulation, previous spontaneous abortion, history of previous ectopic pregnancy and short birth intervals (less than 36 month) were associated directly with miscarriage.

Keywords: Abortion, Case-control study, Iran, Spontaneous

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Introduction

Miscarriage means intentional or spontaneous loss of the fetus; it refers to the premature withdrawal of the pregnancy product (during the first 20 weeks of pregnancy) and before its development (1). The global risk of miscarriage rate has been reported to be 10% to 20% of pregnancies (2,3). Based on the latest report by the World Health Organization (WHO), miscarriage increases the risk of mental disorders in pregnant women by 2.5 times. According to WHO report, the most common complications following abortion are infections, hemorrhage, embolism, and physical problems (4). Previous studies showed that the risk of miscarriage is a function of factors like lifestyle, including diet, maternal smoking, alcohol consumption, and other factors such as obesity, maternal age of 35 years and above, previous history of miscarriage, history of extrauterine pregnancy, and paternal age (5-8).

Despite research on multiple known maternal-related factors, it is unknown in more than 50% of couples (9). In Iran, the miscarriage rate is less available due to its legal limitations, but estimates indicate that more than 5% of maternal mortality is due to abortion and its complications (10).

Previous studies have suggested that chromosomal abnormalities account for more than 50% of miscarriages. Other factors associated with abortion include aging, gynecological infections, diabetes, inadequate progesterone production, polycystic ovary syndrome, maternal factors such as phospholipid antibodies, a history of two or more miscarriages, obesity, smoking, alcohol, and caffeine consumption. Psychological stress is vitamin D deficiency and anti-epileptic drugs (1,11). Other studies have estimated that about 2-3% of miscarriages are related to hypothyroidism (12). The consequences of miscarriage are widespread, including bleeding, shock, and death. Other complications of abortion comprise emotional reactions such as depression, sleep disorders, anger, marital discord (11).

Several studies have been conducted in different countries to investigate the prevalence and risk factors of miscarriage. In Iran, few studies have been conducted on the causes of miscarriage. The risk factors for miscarriage vary in different societies. Thus, the study was conducted to investigate the role of the related factors on miscarriage in the west of Iran.

Materials and Methods

This case-control study was conducted in Zanjan city (Iran) from April 2019 to March 2019. The Research Council of Hamadan University of Medical Sciences approved the study. Zanjan city includes 36 urban health centers.

Women refer to urban health centers for periodic checkups during pregnancy. Health data (such as medical history, physical examination, and routine laboratory tests during pregnancy) for these women was recorded.

The participants of this case-control study were selected among those living in Zanjan (a city located in western Iran) in 2019. The women with miscarriage history were chosen randomly as the case and women with a successful pregnancy history in 2019 as the control. The cases and controls had a pregnancy record in comprehensive urban health service centers. The women with a history of miscarriage at last pregnancy were considered as the case group, and the women with successful pregnancy at later gestation were regarded as a control group. The exclusion criteria were women with a history of intentional abortion and legal abortion. Therefore, women whose health records were incomplete and those having a history of induced abortion or extramarital pregnancy were excluded from the study.

Data were collected by a checklist of contraceptive records available in comprehensive urban health service centers in Zanjan. The checklist had 25 items with demographic characteristics and risk factors for miscarriage. A stillbirth was defined as the birth of a baby with no signs of life at or after 20 weeks' gestation. The birth weight of a live-born infant of less than 2,500 *g*, regardless of gestational age, was defined as the Low Birth Weight (LBW) and more than 4,000 *g* as the High Birth Weight (HBW).

The relationship between each of the independent variables with miscarriage was statistically analyzed using a multiple logistic regression at a 95% confidence level. The backward technique was used for selecting variables. Only those variables whose p-value was≤ 0.20 (in the univariate model) remained in the final

model. Analysis was performed using Stata version 11 (StataCorp, College Station, TX, USA). Informed consent was obtained from the subjects to participate in the study. The ethics committee of the Hamadan University of Medical Sciences approved the study protocol.

Results

During the study period, 219 miscarriages were diagnosed. Controls were selected randomly. The mean (standard deviation) age of the cases and controls were 32.28 (6.45) and 31.26 (5.67) (p=0.020) years, respectively. The characteristics of the study population are given in detail (Table 1).

Table 1. Characteristics of the study population

Variables	Job status	Case (n=219)	Control (n=420)	p-value
Housekeeper		91.3	83.2	
Employed		5.9	12.7	0.041
Student		2.7	4	
Education level (%)				
Primary		19.6	8.6	
Middle school		23.7	16.8	<0.001
High school/diploma		31.5	35.7	
Academic		25.1	38.8	
Total number of pregnancies		2.6±1.01	2.06±1.03	<0.001
Interval between pregnancies (%)				
<3 years		53.9	75.2	<0.001
>3 years		46.1	24.8	
Previous stillbirth history (%)		4.1	2.1	0.154
Previous anemia (%)		4.1	5.9	0.032
Previous s pontaneous abortion (%)		28.3	17.1	<0.001
Previous urinary tract infection (%)		12.3	9.0	0.193
Previous coagulation disorders (%)		2.3	0.5	0.037
Age (years)		32.3±6.4	31.3±5.7	0.020
Previous low birth weight (%)		5.9	10.2	0.068
Previous twin birth (%)		2.7	3.6	0.576
Previous ectopic history (%)		7.3	1.7	0.001>
Previous high birth weight (%)		5.5	6.7	0.557
Previous coronary heart disease history (%)		0.9	0.95	0.961
Previous renal failure (%)		1.8	1.2	0.517
High blood pressure (%)		4.6	1.9	0.054
Impaired thyroid function (%)		15	13.8	0.666
Previous thalassemia history (%)		2.7	1.7	0.362

Table 2. The role of some risk factors on miscarriage according to multivariable logistic regression

Variables	Crude or (95%CI)	p-value	Adjusted or(95%CI)	p-value
Age (Per one-year increase in age)	1.01(1.00,1.05)	0.041	1.02 (0.99,1.05)	0.177
Education (for an increase in a degree)	0.65(0.55,0.77)	<0.001	0.65(0.54,0.77)	<0.001
IBP(>3 years/<3 years)	2.60(1.84,3.76)	<0.001	2.5(1.70,3.7)	<0.001
Previous stillbirth (yes/no)	1.95(0.76,5.0)	0.161	1.28(0.46,3.67)	0.635
Previous spontaneous abortion (yes/no)	1.90(1.29,2.84)	0.001	1.09(0.69,1.71)	0.697
Previous coagulation disease (yes/no)	4.87(0.93,25.31)	0.059	5.80(1.0,33.7)	0.050
Previous anemia (yes/no)	1.92(1.04,3.54)	0.035	1.66(0.86,3.22)	0.130
Previous UTI* (yes/no)	1.41(0.83,2.38)	0.194	1.18(0.67,2.09)	0.557
Previous ectopic (yes/no)	4.65(1.88,11.48)	0.001	3.64(1.3,9.552)	<0.001
High blood pressure (yes/no)	2.46(0.95,6.33)	0.061	1.89(0.67,5.3)	0.225

* UTI: urinary tract infection, IBP: interval between pregnancies.

The mean difference was analyzed by independent t-test and the difference in ratios by Chi-square test.

Results from the logistic regression analysis of several binary and continuous predictors of miscarriage are given in table 2. According to the results, there was a direct association between.

There was an inverse association between miscarriage and educational level (OR=0.65,95%CI:0.54,0.77). The OR of miscarriage was 5.80 (95%CI:1.0-33.7) for those women with a history of previous coagulation disease and 3.64 (95%CI:1.39-9.55) for those with a history of previous ectopic pregnancy. Finally, pregnancy interval less than three years was associated with miscarriage (OR=2.5,95%CI: 1.7,3.7). These four associations were statistically significant.

Previous stillbirth (OR=1.28,p=0.635), previous spontaneous abortion (OR=1.09,p=0.697), prior anemia (OR=1.66,p=0.130), previous Urinary Tract Infection (UTI) (OR=1.18,p=0.557), and high blood pressure (OR=1.89,p=0.225) during pregnancy were related to miscarriage, but the associations were not statistically significant.

Discussion

Miscarriage, also known as spontaneous abortion and pregnancy loss, is a multifactorial complication affected by several risk factors that may vary across communities. The present study revealed the crude and adjusted effect of several predictors that may play a role in miscarriage.

According to the results, miscarriage is directly associated with short birth intervals (less than 36 months). Concerning the role of the gap between pregnancies, it is noteworthy that consecutive pregnancies with short intervals increase the risk of anemia in women and thus disrupt the maternal anemia, oxygen delivery, nutrition, and health of the fetus (13). Rodrigues *et al* (14) reported that short inter-pregnancy intervals increased the risk of miscarriage and fetal death; also, for women of all ages, short intervals between pregnancies were associated with a higher risk for preterm birth and having infants small for their gestational age (15,16). Furthermore, Nonyane *et al* (17) showed that the short inter-outcome intervals after stillbirth, neonatal death and spontaneous abortion were associated with

a high risk of a similar outcome in the next pregnancy. The effect of education was significant in the multivariate logistic regression model. Therefore, with an increase in education, unintentional abortion was reduced by 35%. Higher education is usually connected with a higher economic and social status. In this respect, the women with higher socioeconomic status have higher chances of having lower risk factors than other women, including a better lifestyle, awareness of the need for prenatal care and distance, and proper placement between pregnancies. This result was confirmed by Poorolajal *et al* (18). Also, Vaisanen *et al* demonstrated that women with basic education had a higher likelihood of abortion than women with academic education (19). Miscarriages usually occur in young women under 20 and in low-income countries. Women in developing countries are more likely to be at risk than other women, including low age at delivery, high and short-term pregnancies, premature birth, low income, inappropriate sexual partner, abortion in unsafe conditions, dropping out of school, and improper use of contraceptives (20).

Another influential factor was the history of previous ectopic pregnancy, which was related directly to miscarriage (statistically significant). Ectopic pregnancy is a considerable health problem accounting for about 10% of maternal mortality. Women with a history of Recurrent Spontaneous Abortion (RSA) have a higher frequency of ectopic pregnancy than the general population (21,22).

We found a direct association (with a significant statistically) between previous coagulation disease and miscarriage. Previous studies indicated recurrent miscarriage syndrome caused by blood protein or platelet defects as disorders associated with a hemorrhagic tendency or as defects related to a thrombotic tendency (23,24).

In this study, all the miscarriage cases (which were registered in the comprehensive urban health service centers) during 2020 were included. Thus, the selection bias was minimized.

We indicated that miscarriage was directly associated with several factors, such as previous stillbirth, previous spontaneous abortion, previous anemia, previous UTI, and high blood pressure during pregnancy. This may be attributed to the rarity of these predictors in both cases and controls, and in fact, many previous investigations have shown that miscarriage is associated with most of these factors. In this case-control study, none of the case and control groups of women had a history of smoking and alcohol use. Hence, the analysis of this variable was impossible.

The present study suffered from several critical limitations. Firstly, we used data recorded in health centers, so the quality and accuracy of the results depend on the quality of the recorded data. This might result in information bias. Secondly, due to the nature of case-control studies, the observed effect may not necessarily be causal; thus, overall, a major longitudinal study with appropriate power and more accurate laboratory study is strongly recommended. In this study, the effect of other factors such as diabetes, social class, and income was not studied as a separate factor, so their survey in future studies is recommended.

Conclusion

In the present study, increasing age, low education level, history of previous coagulation, previous spontaneous abortion, history of previous ectopic pregnancy and short birth intervals (less than 36 month), were associated directly with miscarriage.

Ethics approval and consent to participate

This case-control study (Code: IR.UMSHA.REC.1399.386) was approved by the research committee of the Hamadan University of Medical Sciences (UMSHA), Hamadan, Iran.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that there is no conflict of interest.

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References

1. Zhou H, Liu Y, Liu L, Zhang M, Chen X, Qi Y. Maternal pre-pregnancy risk factors for miscarriage from a prevention perspective: a cohort study in China. Eur J Obstet Gynecol Reprod Biol 2016 Nov;206:57-63.

2. Moradinazar M, Najafi F, Nazar ZM, Hamzeh B, Pasdar Y, Shakiba E. Lifetime prevalence of abortion and risk factors in women: evidence from a cohort study. J Pregnancy 2020 Apr 27;2020:4871494.

3. Cohain JS, Buxbaum RE, Mankuta D. Spontaneous first trimester miscarriage rates per woman among parous women with 1 or more pregnancies of 24 weeks or more. BMC Pregnancy Childbirth 2017 Dec 22;17(1):437.

4. Berek JS, Novak s. Gynecology. 13th ed. Philadelphia: Lippincott Williams and Wilkins; 2002. 1432 p.

5. Wang JX, Davies MJ, Norman RJ. Obesity increases the risk of spontaneous abortion during infertility treatment. Obes Res 2002 Jun;10(6):551-4.

6. Metwally M, Ong KJ, Ledger WL, Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. Fertil Steril 2008 Sep;90(3):714-26.

7. Turner MJ, Fattah C, O'Connor N, Farah N, Kennelly M, Stuart B. Body mass index and spontaneous miscarriage. Eur J Obstet Gynecol Reprod Biol 2010 Aug;151(2):168-70.

8. de La Rochebrochard E, Thonneau P. Paternal age and maternal age are risk factors for miscarriage; results of a multicentre European study. Hum Reprod 2002 Jun;17(6):1649-56.

9. du Fosse N, van der Hoorn ML, Eikmans M, Heidt S, le Cessie S, Mulders A, et al. Evaluating the role of paternal factors in aetiology and prognosis of recurrent pregnancy loss: study protocol for a hospital-based multicentre case-control study and cohort study (REMI III project). BMJ Open 2019 Nov 14;9(11):e033095.

10. Mahmoudiani S, Ahmadi A, Javadi A. [The prevalence and influential factors of abortion in the women in the rural areas of fars province, Iran (2015)]. Iran J Nurs 2018;31(115):51-61. URL: http://ijn.iums.ac.ir/article-1-2809-en.html. Persian

11. Wahabi HA, Fayed AA, Esmaeil SA, Bahkali KH. Progestogen for treating threatened miscarriage. Cochrane Database Syst Rev 2018 Aug 6;8(8):CD005943.

12. Zhang Y, Wang H, Pan X, Teng W, Shan Z. Patients with subclinical hypothyroidism before 20 weeks of pregnancy have a higher risk of miscarriage: a systematic review and meta-analysis. PLoS One 2017 Apr 17;12(4):e0175708.

13. Sun D, McLeod A, Gandhi S, Malinowski AK, Shehata N. Anemia in pregnancy: a pragmatic approach. Obstet Gynecol Surv 2017 Dec;72(12):730-7.

14. Rodrigues T, Barros H. Short interpregnancy interval and risk of spontaneous preterm delivery. Eur J Obstet Gynecol Reprod Biol 2008 Feb;136(2):184-8.

15. Nonyane BAS, Norton M, Begum N, Shah RM, Mitra DK, Darmstadt GL, et al. Pregnancy intervals after stillbirth, neonatal death and spontaneous abortion and the risk of an adverse outcome in the next pregnancy in rural Bangladesh. BMC Pregnancy Childbirth 2019 Feb 9;19(1):62.

16. Baqui AH, Ahmed S, Begum N, Khanam R, Mohan D, Harrison M, et al. Impact of integrating a postpartum family planning program into a community-based maternal and newborn health program on birth spacing and preterm birth in rural Bangladesh. J Glob Health 2018 Dec;8(2):020406.

17. Nonyane BA, Norton M, Begum N, Shah RM, Mitra DK, Darmstadt GL, et al. Pregnancy intervals after stillbirth, neonatal death and spontaneous abortion and the risk of an adverse outcome in the next pregnancy in rural Bangladesh. BMC Pregnancy Childbirth 2019 Feb 9;19(1):62.

18. Poorolajal J, Cheraghi P, Cheraghi Z, Ghahramani M, Doosti Irani A. Predictors of miscarriage: a matched case-control study. Epidemiol Health 2014 Nov 20;36:e2014031.

19. Väisänen H. The association between education and induced abortion for three cohorts of adults in Finland. P Popul Stud (Camb) 2015;69(3):373-88.

20. Maravilla JC, Betts KS, Couto ECC, Alati R. Factors influencing repeated teenage pregnancy: a review and meta-analysis. Am J Obstet Gynecol 2017 Nov;217(5):527-545.e31.

21. Gracia CR, Sammel MD, Chittams J, Hummel AC, Shaunik A, Barnhart KT. Risk factors for spontaneous abortion in early symptomatic first-trimester pregnancies. Obstet Gynecol 2005 Nov;106(5 Pt 1):993-9.

22. Webster K, Eadon H, Fishburn S, Kumar G. Ectopic pregnancy and miscarriage: diagnosis and initial management: summary of updated NICE guidance. BMJ 2019 Nov 13;367:l6283.

23. Babker AM. The role of Inherited Blood Coagulation Disorders in Recurrent Miscarriage Syndrome. J Crit Rev 2020;7(1):16-20.

24. Bick RL. Recurrent miscarriage syndrome and infertility caused by blood coagulation protein or platelet defects. Hematol Oncol Clin North Am 2000 Oct;14(5):1117-31.