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Maternal pre-pregnancy risk factors for miscarriage from a prevention perspective: a cohort study in China

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ABSTRACT

Objective: To assess the relationship of the pre-pregnancy modifiable risks with miscarriage.
Study design: We randomly selected 51 communities or villages from January 2013 to December 2014 in Anhui, China. We calculated incidence rate ratios (RR) and 95% confidence intervals (CIs) for each risk factor for miscarriage.
Results: The incidence rate of miscarriage was 7.45%, and pre-embryonic loss account for 12.66%, embryonic loss account for 38%, and fetal losses account for 49.34% of all loss. In multivariate analysis, women with hypertension (RR = 2.272, 95% CI = 1.27–4.04), women had a family history of abortion in their mother (RR = 1.96, 95% CI = 1.22–3.14) prior to pregnancy had significantly higher adjusted risk ratio for miscarriage. Obese, overweight, and underweight prior to pregnancy were about 2.01 (95% CI = 1.1–3.68), 1.71 (95% CI = 1.04–2.81), and 2.05 (95% CI = 1.3–3.23) times more likely to end in miscarriage compared with normal weight. Some physical examination indicators, for example pH value of leucorrhea ≥4.5 (RR = 2.13, 95% CI = 1.48–3.07), red blood cell count <5 10(12)/L (RR = 1.52, 95% CI = 1.02–2.26), and positive LgG antibodies to human cytomegalovirus (RR = 1.45, 95% CI = 1.02–3.14) prior to pregnancy had good prediction effect on miscarriage. We also found remarkable differences on risk factors between non-fetal losses and fetal losses.
Conclusions: Our results suggest that these modifiable risks should be included into pre-conception counseling as important risk factors for screening high-risk population and reducing the rate of spontaneous abortion.

Introduction

Miscarriages is the most common adverse outcome of pregnancy in the word, occurring in 15–20% of clinically recognized pregnancies [1]. Spontaneous abortion is a multi-factorial origin, with acquired or environmental factors probably exceeding genetic factors in its causation [2]. As miscarriages are considered irreversible, prevention is probably the only way to intervene in this problem, and identifying modifiable risk factors for miscarriage is potentially important for public health.

There is considerable literature reporting several modifiable risk factors for miscarriage. Advanced maternal age at conception, obesity, smoking, alcohol and caffeine consumption, lifting of heavy weights, night shift work and psychological stress have all been identified as modifiable risk factors during pregnancy for miscarriage. An estimated 25.2% of miscarriages could be prevented if these risk factors could be attenuated to low-risk levels [3]. Several other potentially modifiable risk factors during pregnancy have been examined in recent conducted cohort studies, such as maternal vitamin D deficiency, use of antiepileptic drugs, and previously diagnosed genital diseases [2,4,5].

However, the majority of published studies on miscarriages were conducted during pregnancy and fewer studies were conducted before pregnancy. The left-truncation bias is common in the studies that recruit women who are already pregnant, because approximately 80% of miscarriage occurs in the first trimester, during an interval over which a woman might not yet have learned of being pregnant or begun prenatal care. For some of the women, the data on risk factors were collected after they had had a miscarriage, making it susceptible to recall bias. Furthermore, a more complete understanding of the relationship between pre-pregnancy modifiable risk factors and miscarriage is important for preconception counseling and public health programs for

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women of reproductive age, these risks and the interventions to prevent and avoid them are an important component of preconception care, nevertheless the information about the pre-pregnancy modifiable risk factors for miscarriage was scarce. Thus, we conducted a large population based cohort study to investigate the pre-pregnancy modifiable risk factors for miscarriage.

Method

Study population

This is a community-based prospective cohort study of the miscarriages in China. This study was conducted in 51 randomly selected communities or villages from January 2013 to December 2014 in Anhui, China. All the participants were enrolled before pregnancy in 2013, and follow-up continued until pregnancy outcomes occurred or for a maximum of 24 months. Women eligible to participate in this cohort study were aged 18–40 years, residents of Anhui, be married, not using fertility treatment, and trying to become pregnant during the next six months. The recruitment of women was completed by the community health services staffs of the selected communities or villages. Women gave informed consent for all aspects of the study, which was approved by the Ethical Committee. The research protocol was reviewed and approved by the Ethic Committee of the First Affiliated Hospital of Bengbu Medical College.

Data collection and follow-up

At the time of enrollment, all participants were asked to complete a structured questionnaire about the demographics, lifestyle and behavioral factors, and reproductive and medical history. Women were also encouraged to seek antenatal care in the appointed health facilities once they were pregnant. The baseline questionnaire collected information including maternal age ($\leq$25 years, 25–29 years, 30–34 years, $\geq$35), smoking (non-smoking, current smoking), alcohol consumption (never drinking, current drinking), social status defined by education (primary education, secondary education, tertiary level), ethnicity (Han nationality, other ethnicity), parity (nulliparous, multiparous), abortion history (never, have more than one times), stress in life (no stress in life, have stress in life), contraception measures (never use contraception measures, using intrauterine device, using other contraception), previously diagnosed diseases (genital diseases, hypertension, diabetes mellitus), and so on. All participants were received a free complete examination including an ultrasound examination, general physical examination, blood routine examination, routine urine test, leucorrhea routine inspection, and testing of infection status of HIV (human immunodeficiency virus), HBV (hepatitis B virus), cytomegalovirus, and rubella virus.

Pre-pregnant BMI is calculated by dividing weight in kilograms by height in meters squared. The BMI classification for adults is defined by fixed cut-off points: a BMI of less than or equal to 18.5 is considered underweight; 18.6–23.9 is considered normal weight; from 24 to 27.9 is considered overweight; above 28 is considered obesity.

All participants were required to provide name, a valid mobile phone number, detailed home address, and national identification number for following-up. To obtain information on pregnancy status and pregnancy outcomes, the trained health care workers responsible for contacting all the participants every month by telephone with a follow-up questionnaire. Follow-up questionnaire was mainly used to collect pregnancy status, including whether any clinically recognized pregnancy losses had occurred.

Table 1
Socio-demographic characteristics of women in this cohort study.

Variables	Frequency	Percentage
Age (in years)		
$\leq$24	1213	39.46
25–29	1280	41.64
30–34	382	12.43
$\geq$35	199	6.47
Educational status		
Primary education	2563	83.38
Secondary education	335	10.90
Tertiary level	176	5.73
Ethnicity		
Han nationality	2939	95.61
Others	135	4.39
Pre-pregnancy BMI		
Underweight (<18.5)	449	14.61
Normal (18.5–23.9)	2154	70.07
Overweight (24–27.9)	326	10.61
Obese ($\geq$28)	145	4.72
Smoking status		
Non-smoker	3065	99.71
Current smoker	9	0.29
Alcohol use status		
Never drinking	3051	99.25
Current alcohol use	23	0.75
Parity		
Nulliparous	1995	64.90
Multiparous	1079	35.10
Spontaneous abortion history		
Yes	195	6.34
No	2879	93.66
Induced abortion history		
Yes	651	21.18
No	2423	78.82
Family history of abortion in their mother		
Yes	252	8.23
No	2810	91.77

Definition and category of miscarriage

We defined miscarriage as a spontaneous fetal death and/or expulsion before 20 completed weeks of gestation. According to the ultrasound findings and pregnant weeks, miscarriage was divided into three categories in this study: (1) pre-embryonic loss was defined as pregnancy loss before 5 weeks of gestation with an empty gestational sac or a yolk sac; (2) embryonic losses was defined as pregnancy loss at 6–9 week of gestation with a detectable embryo, measuring less than the corresponding size for 10 weeks' gestation; (3) fetal losses was defined as pregnancy loss at 10–20 week of gestation a crown–rump length >30 mm or other biometry [6].

Statistical analysis

Absolute rates of miscarriage and 95% confidence interval were calculated by dividing the number of miscarriage by the total person of follow-up. To determine which factors were associated with an increased risk of miscarriage, we calculated Risk ratios (RR) and its 95% confidence intervals (CIs) for each risk factor for miscarriage using a Poisson regression model. RR for miscarriage were adjusted for maternal age, educational status, pre-pregnancy BMI, parity, miscarriage history, hypertension status, stress status in life, the status of using contraception measures, leucorrhea routine inspection result, blood routine examination result, antibody test result of cytomegalovirus. Statistical analyses were conducted using SAS, version 9.3 (SAS Institute, Inc., Cary, NC) and $P < 0.05$ was considered statistically significant.

Results

Table 1 shows the selected characteristics of women in the cohort. 41.64% of the women were 25–29 years old, 83.38% of the