Teenage pregnancy as a risk factor for placental abruption: Findings from the prospective Japan Environment and Children's Study

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Abstract

Objective: To examine the effect of maternal age on placental abruption Design: Prospective cohort study Setting: Fifteen regional centers across Japan Population: We identified 94,410 Japanese women (93,994 without placental abruption and 416 with placental abruption) who were recruited in the Japan Environment and Children's study between January 2011 and March 2014. Methods: Multiple regression models were used to identify whether maternal age (<20 years, 20–24 years, 25–29 years, 30–34 years, and [?] 35 years) is a risk factor for placental abruption. The analyses were conducted while considering history of placental abruption, assisted reproductive technology, number of previous deliveries, smoking during pregnancy, body mass index before pregnancy, chronic hypertension, and uterine myoma as confounding factors. Main outcome measures: Maternal age as a risk factor for placental abruption Results: Besides advanced maternal age ([?]35 years; adjusted odds ratio [aOR]: 1.7, 95% confidence interval [CI]: 1.1–2.5), teenage pregnancy was also a risk factor for placental abruption (aOR: 2.8, 95% CI: 1.2–6.5) when maternal age of 20–24 years was set as a reference. Conclusions: In the Japanese general population, besides advanced maternal age, teenage pregnancy was also a strong risk factor for placental abruption. The maternal age in Japan is changing since recent decades. Therefore, it is important for obstetric care providers to provide proper counseling to young women based on the up-to-date evidences. Funding: The Japan Environment and Children's Study was funded by the Ministry of the Environment, Japan

Introduction

Placental abruption is a significant obstetric complication that affects both maternal and neonate mortality and morbidity. It is defined as the premature partial or total separation of a normally implanted placenta.[1] Maternal consequences include excessive blood loss and disseminated intravascular coagulation (DIC), which sometimes needs blood transfusion and can lead to hypovolemic shock, multiorgan failure, peripartum hysterectomy, and rarely, death.[2,3] Neonatal consequences include preterm birth and related hypoxia or an asphyxia condition.[1,4] Fetal asphyxia combined with prematurity can be associated with short-term sequelae such as neonatal encephalopathy/hypoxic-ischemic encephalopathy and long-term sequelae such as cerebral palsy, lung diseases, and epilepsy.[1,5]

The prevalence of placental abruption varies across regions. In some countries, the prevalence of placental abruption is increasing, possibly due to changes in the risk factors,[2] including increasing maternal age, body mass index, and increasing use of assisted reproductive technology (ART) since the past decade. Maternal age is one of the key risk factors for placental abruption. In 1993, a prospective cohort study comprising 30,681 participants with singleton pregnancies reported that the risk of placental abruption increased in a year (odds Ratio [OR] 1.03, 95% confidential interval [CI] 1.00–1.06, p = 0.04).[6]The statistic reports suggest that the mean maternal age is increasing in Japan.[7]Although a recent Japanese birth cohort study reported that increasing maternal age is a risk factor for preterm delivery and fetal growth restriction,[8]teenage maternal age is also a risk factor for severe maternal obstetric complications such as hypertensive disorders of pregnancy (HDP) and placental abruption.[9] Owing to the changes in social background during the last decade, up-to-date evidence for the effect of maternal age on placental abruption is required.

Several studies have focused on the advanced maternal age as a risk factor for placental abruption. However, a few prospective studies have comprehensively assessed both teenage and advanced maternal age as risk factors for placental abruption, while accounting for several confounding factors using a large number of participants. Therefore, the present study, including the participants from the largest prospective birth cohort study in the Japanese population conducted between 2011 and 2014, examined the effect of maternal age on placental abruption.

Methods

In the present study, we investigated the data of the Japan Environment and Children's Study (JECS), which is a nationwide, government-funded, birth cohort study[10] that was started in January 2011 to investigate the effects of environmental factors on children's health. The eligibility criteria for the JECS participants (expectant mothers) were as follows: (1) residing in one of the study areas at the time of recruitment and expected to reside continually in Japan for the foreseeable future, (2) an expected delivery date between August 01, 2011 and mid-2014, and (3) the ability to participate in the study without difficulty (i.e., the participant needed to be able to comprehend the Japanese language and complete the self-administered questionnaires). This study was conducted in 15 Regional centers across Japan as described previously.[10] The JECS protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and by the ethics committees of all participating institutions. The JECS was conducted in accordance with the principles of Declaration of Helsinki and other nationally valid regulations and guidelines. Written informed consent was obtained from all participating women. There was no patient and public involvement in this study.

Data collection

The current analysis used the JECS dataset released in June 2016 (dataset: jecs-ag-20160424). We used two types of data: (1) T1, comprising data obtained from the self-reported questionnaires collected during the first trimester (the first questionnaire), and included questions related to the maternal medical background; (2) M0, which included data for obstetric outcomes. These data were retrieved from the medical records provided by each cooperating health care provider. The participants with multiple-gestation pregnancies and those with missing data were excluded from the analysis.

Maternal medical background

The maternal medical background information was obtained from the M0 data, which included information on maternal age at the time of delivery, pre-pregnancy body mass index (BMI), the presence of maternal chronic hypertension, and parity; and T1 data, which included information on previous pregnancy complication, maternal smoking status, manner of conception, and pre-pregnancy presence of uterine myoma. The method of conception was categorized as natural or ART-related, with ART defined as conception after in vitro fertilization (IVF) and/or intracytoplasmic sperm injection (ICSI); or cryopreserved, frozen, or blastocyst embryo transfers.[11] The mothers were categorized into the following five groups based on the age: <20 years, 20–24 years, 25–29 years, 30–34 years, and [?]35 years. The mothers were also stratified based on the number of previous deliveries, as follows: 0, 1, 2, 3, and [?]4. BMI was calculated according to the criterion of World Health Organization (body weight [kg]/height^2 [m^2]). We further categorized the participants into three groups according to their BMI: <18.5 kg/m^2, 18.5–25.0 kg/m^2, and [?]25.0 kg/m^2. A self-reported questionnaire during the first trimester provided information on the participants' smoking habit as follows: "Never," "Previously did, but quit before realizing current pregnancy," "Previously did, But quit after realizing current pregnancy," and "Currently smoking." The women in "Currently smoking" category were considered as smokers and comprised the smoking category, while the others were considered as non-smokers and comprised the non-smoking category. Maternal participants were also asked to answer the question:

"Have you ever been diagnosed as having a uterine myoma in a medical institution?" The participants who answered "yes" were classified as having a uterine myoma. Maternal chronic hypertension was defined as the presence of hypertension before conception. The process of collecting data for pre-pregnancy gynecological complications from the self-reported questionnaire of JECS has been validated previously.[12,13]

Obstetrical outcomes

The data for obstetrical outcomes were obtained from the M0 data and included the following: gestational age at the time of delivery, the presence or absence of placental abruption, mode of delivery, umbilical artery (UmA) pH, and maternal transfusion. The mode of delivery was categorized into vaginal delivery or cesarean section (CS). In the present study, placental abruption was diagnosed clinically based on the clinical findings of abdominal pain, vaginal bleeding, uterine contractions, fetal distress, and vital signs' abnormalities at the discretion of the obstetrician in charge. Histological confirmation was not mandatory for the diagnosis of placental abruption during the present analysis. Fetal arterial blood was obtained from the site of delivery, and UmA pH was measured immediately after delivery. Fetal acidosis was stratified by UmA pH <7.20, <7.10, or <7.00 based on a previous study, which reported that the UmA pH threshold of 7.20 was associated with an increased risk of adverse short-term outcomes,[14] UmA pH threshold of 7.10 was associated with an increased risk of adverse neurological sequelae,[15] and cerebral palsy was more frequent at UmA pH <7.00.[16]

Statistical analyses

The data of the women with placental abruption were reviewed. The maternal background and obstetric outcomes were compared between women with and without placental abruption. We also examined the frequency of placental abruption according to the gestational age. The chi-square test and Fisher's exact test were used to compare the categorical variables, and t-test was used to compare the continuous variables after confirming that each of the continuous variables was normally distributed. The adjusted OR (aOR) and 95% CI for placental abruption were calculated using the multiple logistic regression model. The ORs were adjusted for confounding variables, including history of placental abruption, ART pregnancy, parity, maternal age, smoking during pregnancy, BMI before pregnancy, chronic hypertension, and uterine myoma. In the logistic regression model, dummy variables were used for the categorical variables that consisted of more than three categories. All statistical analyses were conducted using SPSS, version 26 (IBM Corp., Armonk, NY, USA). The differences with P <0.05 were considered statistically significant.

Results

In total, 104,102 records were identified during the study period. Of those, 1,994 records from women with multiple gestation pregnancies and 7,698 records of women with missing data were excluded from the analysis (Figure 1). After applying our exclusion criteria, the data of 94,410 maternal participants were included in the analysis. Among 94,410 participants, 416 women had placental abruption and 93,994 women were without placental abruption. The prevalence rate of placental abruption was 0.4% (416/94410). Almost half (44.1%) of the placental abruption cases occurred prematurely before the gestational age of 37 weeks (Figure 2A).

Table 1 summarizes the maternal characteristics and obstetric outcomes of the participants stratified by the presence and absence of placental abruption.

The rate of CS in women with placental abruption was 62.2%, which was significantly higher than that in women without placental abruption (18.6%, P <0.001). Among women with placental abruption, the rate of CS dropped rapidly after 37 weeks of pregnancy (Figure 2B).

Table 2 shows the results of the logistic regression analyses. After adjusting for potential confounding factors, history of placental abruption (aOR: 3.5, 95% CI: 1.3–9.6, P =0.013), ART (aOR: 1.7, 95% CI: 1.1–2.7,P =0.021), maternal age <20 years (aOR: 2.8, 95% CI: 1.2–6.5, P =0.016), maternal age [?]35 years (aOR: 1.7, 95% CI: 1.1–2.5, P =0.024), smoking during pregnancy (aOR: 1.7, 95% CI: 1.2–2.5, P =0.003), and chronic hypertension before pregnancy (aOR: 4.0, 95% CI: 2.5–6.2, P <0.001) were associated with placental abruption. When no parity was set as a reference, no association was observed between the number of parities and risk of placental abruption.

Discussion

Main findings

To the best of our knowledge, this is the first study to elucidate the risk factors for placental abruption based on the data of a large cohort study conducted in Japan. Consistent with several studies, the present study demonstrated that history of placental abruption, ART pregnancy, smoking during pregnancy, chronic hypertension, and maternal age were the risk factors for placental abruption. We also found that compared to advanced maternal age, teenage maternal age was more strongly associated with placental abruption. The number of previous deliveries was not associated with the incidence of placental abruption.

Interpretation

The prevalence of placental abruption varies across regions. In the present study, the incidence of placental abruption was 0.4%, which is similar to that reported in the Nordic countries (0.4–0.5%) and is lower than that reported for the US (0.6–1.0%).[2]Postpartum hemorrhage (PPH) is the most frequently reported maternal morbidity associated with the placental abruption, and PPH, as a consequence of placental abruption, elevates the incidence of maternal blood transfusion. The rate of transfusion due to placental abruption in the present study was 1.7%, which is lower than that reported in the previous studies (2.4–14.6%).[1] The distinctive difference in maternal transfusion rate for women with placental abruption may due to different diagnosis criteria for placental abruption in each study. The diagnosis of abruption is primarily clinical, but sometimes findings from the imaging, laboratory, and postpartum pathologic studies can be used to support the clinical diagnosis.[1] However, to date, there is no gold standard for diagnosing placental abruption.

The findings of the present study indicate that half of the placental abruption cases occurred before the 37 weeks of gestation. Preterm birth (PTB) is one of the most frequently reported obstetric outcomes associated with the placental abruption.[1] PTB has two clinical subtypes, viz., spontaneous PTB and medically indicated PTB; the latter occurs due to HDP.[8] Placental abruption can lead to both spontaneous and medically indicated PTB. Spontaneous PTB due to placental abruption is thought to be the result of bleeding from the separation of the placenta, which irritates the uterine lining and stimulates uterine contractions leading to PTB.[17]Medically indicated PTB because of placental abruption is usually conducted by CS to reduce the risk of maternal and perinatal morbidity and mortality.[18] The present study showed high prevalence of CS (62.2%) for cases with placental abruption, and high percentage of CS was before 37 weeks of gestation (Figure 2B), suggesting that most cases of PTB were medically indicated.

Placental abruption is a complex complication of pregnancy. Although several risk factors for placental abruption are known, its etiopathogenesis is not fully understood. Ananth et al. reported that instead of the number of previous deliveries, the maternal age was an independent risk factor for placental abruption.[19] The findings of the present study are consistent with those reported by Ananth et al. The underlying reason for why advanced maternal age increases the risk of placental abruption is speculative. Most abruptions appear to be related to a chronic placental disease process, wherein, abnormalities in the early development of the spiral arteries, which could be affected by maternal age, can lead to decidual necrosis, placental inflammation, and possibly infarction, ultimately resulting in vascular disruption and bleeding.[20–22] A few studies have reported the association between teenage pregnancy and placental abruption. Kyozuka et al., using descriptive analysis, reported that maternal age <20 years is responsible for the highest occurrence of severe maternal complications such as HDP and placental abruption.[9] They concluded that low socio-economic status of teenagers could be associated with the high occurrence of severe maternal complications. The underlying reason for why teenage pregnancy is an independent risk factor for placental abruption in the present analysis is more speculative. However, the findings of the present study must be interpreted with caution because teenage women are likely to be associated with less education, low income, and malnutrition, which have not been considered as confounding factors in the present analysis. The placental abruption during teenage could be due to direct mechanical events such as blunt abdominal trauma and/or rapid uterine decompression, which are more eventful in young maternal age.[23]

Strengths and limitations

The strength of the present study is that it is the first large-scale, nationwide, birth cohort study in Japan that investigated various factors contributing to placental abruption in pregnant women. Therefore, the findings of this study can be considered to be representative of the general pregnant population in Japan.[24] The prospective data were collected by the physicians, midwives, nurses, and trained research coordinators, and therefore, are more likely to be accurate.

This study also has a few limitations. First, this study lacked the definition of placental abruption along with the data for type (occurred during antepartum or intrapartum) and severity. The severity of placental abruption could have been graded based on the maternal (DIC, hypovolemic shock, renal failure), fetal (non-reassuring fetal status, intrauterine fetal growth restriction, intrauterine fetal death), or neonatal (preterm delivery, small for gestational age, or neonatal death) complications.[25] The severity usually causes the premature placental separation. Second, regarding the maternal background data, we relied on a self-reported questionnaire instead of objective measurements of uterine myoma before pregnancy. As such, we were not aware of the size and location of uterine myoma. Third, the specific ART methods (IVF and/or ICSI; cryopreserved, frozen, or blastocyst embryo transfer) were not classified in this study. Finally, although we accounted for several confounding factors based on the questionnaire, unknown risk factors for placental abruption might have existed. Further studies are warranted to elucidate the potential impact of these confounding factors on placental abruption and how these factors can impact the clinical practice of all obstetric care providers.

Conclusion

Conventionally, aging is thought to be a risk factor for placental abruption. Therefore, we focused on advanced maternal age for accessing maternal obstetric complications. The findings of the present study suggest that young maternal age is more significantly associated with placental abruption than the advanced maternal age. Owing to the changes in social background during the last decade, an increase in mean maternal age has been observed, along with the advances in ART, and an increasing number of women pursuing higher education and careers[8]; therefore, it is important for obstetric care providers to provide proper counseling to young women based on the up-to-date evidences.

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Disclosure of Interests

The authors declare that they have no competing interests.

Contribution to Authorship

H.K. initiated the concept and designed the study. H.K., E.Y., T.F., T.M., A.K., Sh.Y., A.Y., H.N., K.F., and K.H. provided advice regarding the design of the study. A.S. and Y.O. collected the data. H.K. analyzed the data and wrote the manuscript. M.H., K.F., Se.Y., M.K., A.S., Y.O., K.H., and the JECS group reviewed the manuscript and provided critical advice. All authors approved the final manuscript.

Details of Ethical Approval

The Japan Environment and Children's Study protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies and by the Ethics Committees of Fukushima Medical University (Approved date: May/2014. No1165).

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Table 1 . Basic characteristics of the participants stratified by the presence and absence of placental abruption

Variable	Placental abruption (+) N=416	Placental abruption (-) N=93,994	*P* value

Maternal age (years), mean (SD)	32.0 (5.2)	31.2 (5.0)	0.003[a]
Maternal age category, %			
[?]19 years	1.7	0.8	0.001[b]
20 – 24 years	6.5	8.9	
25 – 29 years	20.9	27.5	
30 – 34 years	37.3	35.5	
[?]35 years	33.7	27.3	
Parity, %			
0	40.9	40.2	0.458[b]
1	35.5	39.1	
2	19.0	16.3	
3	3.6	3.5	
[?] 4	1.2	1.0	
History of placental abruption, %	1.0	0.2	0.021[c]
ART pregnancy, %	5.5	2.9	0.002[b]
Smoking during pregnancy, %	7.9	4.9	0.004[b]
Chronic hypertension, %	5.3	1.3	< 0.001[b]
Uterine myoma, %	6.3	6.1	0.894[b]
BMI, %			
< 18.5 kg/m^2	17.3	16.1	0.144[b]
18.5 – 24.9 kg/m^2	69.3	73.1	
[?] 25 kg/m^2	13.4	10.8	
Obstetric outcomes			
Cesarean section, %	62.2	18.6	< 0.001[b]
UmA pH, mean (SD)	7.21 (0.18)	7.32 (0.12)	< 0.001[a]
UmA pH < 7.20, %	30.7	6.2	< 0.001[b]
UmA pH < 7.10, %	16.1	1.1	< 0.001[b]
UmA pH < 7.00, %	10.9	0.2	< 0.001[b]
Maternal transfusion, %	1.7	0.5	0.004[c]
Maternal transfusion, %	1.7	0.5	0.004[c]

Abbreviations: SD: Standard deviation; ART: Assisted reproductive technology; BMI: Body mass index; UmA: Umbilical artery

[a] *P* value from t-test

[b] *P* value from Chi-square test

[c] *P* value from Fisher's exact test

P <0.05 indicates statistical significance

Table 2. Factors associated with placental abruption: Results from univariate and multivariate logistic regression analyses

Variable	Univariate analysis	Univariate analysis	Univariate analysis	Multivariate analysis	M

	OR	95% CI	P value	aOR	95
History of placental abruption	3.9	1.5 – 10.7	0.007	3.5	1.
ART pregnancy	2.0	1.3 – 3.0	0.002	1.7	1.
Parity					
0	Ref			Ref	
1	0.9	0.7 – 1.1	0.303	0.9	0.
2	1.1	0.9 – 1.5	0.315	1.1	0.
3	1.0	0.6 – 1.7	0.956	0.9	0.
4	1.2	0.5 – 3.0	0.648	1.0	0.
Maternal age, years					
< 20	2.9	1.2 – 6.6	0.013	2.8	1.
20 – 24	Ref			Ref	
25 – 29	1.0	0.7 – 1.6	0.834	1.1	0.
30 – 34	1.4	1.0 – 2.2	0.078	1.5	1.
35	1.7	1.1 – 2.6	0.012	1.6	1.
Smoking during pregnancy	1.7	1.2 – 2.4	0.004	1.7	1.
BMI					
< 18.5 kg/m^2	1.1	0.9 – 1.5	0.346	1.2	0.
18.5 – 24.9 kg/m^2	Ref			Ref	
25 kg/m^2	1.3	1.0 – 1.8	0.062	1.1	0.
Chronic hypertension	4.3	2.8 – 6.7	< 0.001	4.0	2.
Uterine myoma	1.0	0.7 – 1.5	0.894	0.9	0.

Abbreviations: OR: Odds ratio; CI: Confidence interval; aOR: Adjusted odds ratio; ART: Assisted reproductive technology; Ref: Reference; BMI: Body mass index

Figure legends

Figure 1. Flowchart for enrolment and inclusion of participants in the analysis

Figure 2. **(A)** The prevalence of placental abruption stratified by gestational age. **(B)** The rate of cesarean section among women with placental abruption stratified by gestational age.

Figure 1

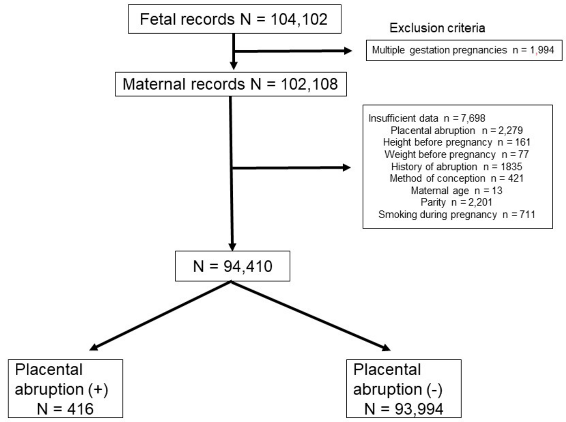
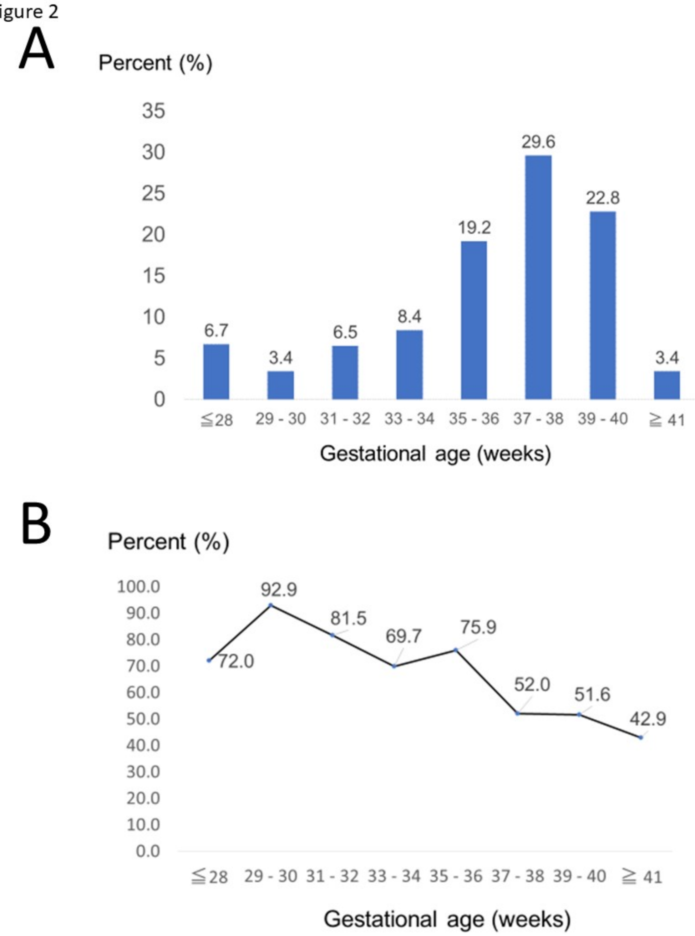

Fetal records N = 104,102
Exclusion criteria
Multiple gestation pregnancies n = 1,994
Maternal records N = 102,108
Insufficient data n = 7,698
Placental abruption n = 2,279
Height before pregnancy n = 161
Weight before pregnancy n = 77
History of abruption n = 1835
Method of conception n = 421
Maternal age n = 13
Parity n = 2,201
Smoking during pregnancy n = 711
N = 94,410
Placental abruption (+) N = 416
Placental abruption (-) N = 93,994

Figure 2


A
Percent (%)
35
30
25
20
15
10
5
0
6.7
3.4
6.5
8.4
19.2
29.6
22.8
3.4
≦28
29 - 30
31 - 32
33 - 34
35 - 36
37 - 38
39 - 40
≧ 41
Gestational age (weeks)
B
Percent (%)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
72.0
92.9
81.5
69.7
75.9
52.0
51.6
42.9
≦28
29 - 30
31 - 32
33 - 34
35 - 36
37 - 38
39 - 40
≧ 41
Gestational age (weeks)