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Original Article

Risk factors for iron deficiency and iron deficiency anemia in pregnant women from plateau region and their impact on pregnancy outcome

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Abstract: Objective: To explore the risk factors for iron deficiency (ID) and iron-deficiency anemia (IDA) in pregnant women from plateau region and their impact on pregnancy outcome. Methods: A retrospective study was conducted on 1,206 pregnant women admitted to the Department of Obstetrics and Gynecology of Qinghai Red Cross Hospital from January 2016 to October 2021. Among them, 721 women were diagnosed with ID and 104 women with IDA. We analyzed the potential risk factors for ID and IDA and also observed the impact of ID and IDA on the pregnancy outcome. Results: Multivariate regression analyses showed that the risk factors for ID were age over 35 years old, number of pregnancies ≥2, number of childbirths >1, number of abortions ≥3 and drinking of strong tea or coffee, while the protective factors against ID were regular prenatal cares, iron supplementation and nutrition guidance during pregnancy. The risk factors for IDA were age ≥35 years old, number of abortions ≥3 and drinking of strong tea or coffee, while the protective factors against IDA were regular prenatal cares and iron supplementation during pregnancy. The incidences of gestational hypertension, fetal distress, preterm birth, cesarean section, postpartum hemorrhage and neonatal asphyxia in the IDA group were higher than those in the non-ID group (all $P<0.05$). Also, the incidences of gestational hypertension, cesarean section and postpartum hemorrhage were higher in the IDA group than those in the ID group (all $P<0.05$). Moreover, the incidences of gestational hypertension, cesarean section and postpartum hemorrhage in the ID group were higher than those in the non-ID group (all $P<0.05$). Conclusion: Pregnant women from the plateau region show a high incidence of ID and IDA, especially elderly parturient women or those with multiple pregnancies, child births or abortions. To reduce the incidence of ID and IDA as well as to improve the pregnancy outcome, our findings suggest pregnant woman to have regular prenatal care and a proper diet by avoiding strong tea or coffee, supplementing iron and receiving nutritional guidance.

Keywords: Pregnancy, iron deficiency, iron deficiency anemia, risk factors, pregnancy outcome

Introduction

Anemia is a common medical complication in pregnant women. The main causes of anemia in pregnancy are iron deficiency (ID), aplastic anemia, globulin production disorder, folic acid deficiency and vitamin B12 deficiency, etc. Among these, ID is the most common and can lead to a series of adverse pregnancy outcomes. Both ID and iron deficiency anemia (IDA) are common clinical diseases in pregnant women. A study showed that the incidence of ID and IDA during pregnancy can be as high as 80% and 20.4%, respectively [1]. According to the World Health Organization, the worldwide prevalence of IDA during pregnancy is 41.8%, in which 23.0% in developed countries, 52.0% in developing countries, and about 10%-40% in China [2]. Anemia during pregnancy can cause stress reactions in pregnant women and fetuses, increase the synthesis of corticotropin-releasing hormone in the body, lead to the secretion from T and B cells, and inhibit the activity of neutrophils and macrophages. Anemia can then reduce the resistance to external bacteria of pregnant women, causing adverse events such as premature rupture of membranes and premature birth [3]. Hence, understanding the factors influencing the occurrence of ID and IDA in women during pregnancy and intervening aggressively can have a positive impact on pregnancy outcomes and prog-

nosis. Previous studies have shown a difference in the incidences of ID and IDA in pregnant women from different regions due to the varying diet, income levels and living habits [4, 5]. Therefore, relevant intervention measures should be developed based on local population characteristics to improve maternal and child health. It should be of great significance to formulate corresponding preventive measures according to the risk factors for ID and IDA during pregnancy in different regions. However, at present, there is no research on risk factors for ID and IDA and their impact on the pregnancy outcome for pregnant women from plateau regions. Thus, this study was designed to explore the risk factors for ID and IDA and their impact on the pregnancy outcome in pregnant women from a plateau region in order to provide reference for the prevention and treatment of ID and IDA during pregnancy.

Materials and methods

General data

In this retrospective study, 1,206 pregnant women admitted to the Department of Obstetrics and Gynecology of Qinghai Red Cross Hospital from January 2016 to October 2021 were enrolled. Among them, 721 women were diagnosed with ID and 104 with IDA. The subjects were aged 19-43 years old, with an average age of 29.6±8.9 years old. This study was approved by the Ethics Committee of Qinghai Red Cross Hospital.

Inclusion & exclusion criteria

Inclusion criteria: (1) Pregnant women with an age of over 18 years old; (2) pregnant women with conditions that met the diagnostic criteria of ID or IDA (ID: serum ferritin <20 μg/L, IDA: hemoglobin <110 g/L and serum ferritin <20 μg/L) [6]. (3) Pregnant women with intrauterine single pregnancy, which was confirmed by B ultrasound; (4) pregnant woman with clear consciousness and normal communication ability; (5) pregnant woman who participated this study voluntarily.

Exclusion criteria: (1) Pregnant women with anemia caused by other reasons; (2) pregnant women with incomplete clinical data; (3) pregnant women with other blood diseases; (4) pregnant women with anemia before the pregnancy; (5) pregnant women who was not able to cooperate the follow-up.

Data collection

Clinical and dietary data, including age, the number of pregnancies, the number of childbirths, the number of induced abortions, the body mass index, the education level, the living area, the family income (per month), regular prenatal cares (≥1 prenatal care (s) per month during pregnancy), vegetarian dominated diet (based on the patient's daily diet record, over 50% of fruit and vegetable intake was defined as vegetarian dominated diet), iron supplementation during pregnancy (*Gynecology and Obstetrics* points out that at least 4 mg of iron is required per day for pregnant women, and they can develop ID or IDA if the amount of iron from the daily diet cannot meet the demand and no iron treatment is given), drinking of strong tea or coffee (≥3 times per week, with a total amount of over 500 mL) and nutrition guidance during pregnancy [4-6] were collected. Additionally, the pregnancy outcome of the included pregnant women was recorded.

Research content

Univariate analysis of variance and multivariate logistic regression were used to analyze the potential risk factors for ID and IDA.

The pregnancy outcome among different groups were compared.

Statistical methods

The statistical software SPSS 17.0 was used to analyze the data. Measurement data conforming to a normal distribution were expressed as mean ± standard deviation ($\bar{x}$ ± sd), and those not conforming to a normal distribution were expressed as M (P25, P75). Independent sample t-test was used for intergroup comparison of the measurement data conforming to normal distribution and homogeneity of variance, expressed as t. The count data were subjected to Pearson chi-square test and expressed as χ^2. Analysis of variance was adopted for the comparison of multiple rates to identify if there was a difference. Bonferroni test was further used for pairwise comparison on the basis of the chi-square test. Logistic regression was used to analyze the potential risk factors for ID and IDA.

Table 1. Potential risk factors for ID in pregnant women (n, %)

Item	ID group (n=721)	Non-ID group (n=485)	χ^2/t	P
Age (years)				
≥35	65 (9.02)	19 (3.92)	11.628	0.001
<35	656 (90.98)	466 (96.08)		
Number of pregnancies (n)				
1	299 (41.47)	259 (53.40)	16.605	<0.001
≥2	422 (58.53)	226 (46.60)		
Number of childbirths (n)				
First	299 (41.47)	259 (53.40)	16.605	<0.001
>1	422 (58.53)	226 (46.60)		
Body mass index (kg/m^2)				
≥18.5	627 (86.96)	409 (84.33)	1.666	0.198
<18.5	94 (13.04)	76 (15.67)		
Education level (n)				
High school or above	622 (86.27)	432 (89.07)	1.823	0.177
Below high school	99 (13.73)	53 (10.93)		
Number of abortions (n)				
0	119 (16.50)	215 (44.33)	113.625	<0.001
1-2	503 (69.77)	235 (48.45)		
≥3	99 (13.73)	35 (7.22)		
Monthly family income (yuan)				
≥5000	434 (60.19)	337 (69.48)	10.853	0.001
<5000	287 (39.81)	148 (30.52)		
Regular prenatal care (n)				
Yes	522 (72.40)	425 (87.63)	39.879	<0.001
No	199 (27.60)	60 (12.37)		
Vegetarian dominated diet (n)				
Yes	391 (54.23)	184 (37.94)	30.852	<0.001
No	330 (45.77)	301 (62.06)		
Iron supplementation during pregnancy (n)				
Yes	137 (19.00)	204 (42.06)	76.031	<0.001
No	584 (81.00)	281 (57.94)		
Drinking of strong tea or coffee (n)				
Yes	194 (26.91)	44 (9.07)	58.226	<0.001
No	527 (73.09)	441 (90.93)		
Nutritional guidance during pregnancy (n)				
Yes	332 (46.05)	348 (71.75)	77.907	<0.001
No	389 (53.95)	137 (28.25)		

Note: t is the statistical value of the t-test; χ^2 is the statistical value of the chi-square test. ID: iron deficiency.

A difference of P<0.05 was considered statistically significant.

Results

Risk factors for ID in pregnant women

As compared with the non-ID group, the ID group had more subjects with an age over 35 years old, number of pregnancies >2, number of childbirths >1, abortions, a monthly income of less than 5000 yuan, a vegetarian-dominated diet and a habit of drinking strong tea or coffee (all P<0.01), while had less subjects with iron supplementation and nutritional guidance during pregnancy (both P<0.001). See **Table 1**.

Table 2. Assignment of potential risk factors for ID in pregnant women

Factor	Independent variable	Assignment
Age (years)	X1	≥35 years old =1, <35 years old =0
Number of pregnancies	X2	≥2=1, 1=0
Number of childbirths	X3	1 or more births =1, first birth =0
Number of abortions	X4	≥3=1, 0-2=0
Monthly family income (yuan)	X5	<5000=1, ≥5000=0
Regular prenatal care	X6	No=1, Yes=0
Vegetarian dominated diet	X7	Yes=1, No=0
Iron supplementation during pregnancy	X8	No=1, Yes=0
Drinking of strong tea or coffee	X9	Yes=1, No=0
Nutritional guidance during pregnancy	X10	No=1, Yes=0

Note: ID: iron deficiency.

Table 3. Multivariate logistic regression analysis of risk factors for ID during pregnancy

Factor	β	SE	Wald value	OR value (95% CI)	P
Age (years)	1.925	0.562	13.287	7.902 (1.962-13.922)	0.002
Number of pregnancies	1.172	0.467	7.692	1.572 (1.245-2.078)	0.027
Number of childbirths	1.178	0.907	10.157	1.358 (1.278-2.093)	0.015
Number of abortions	2.783	0.482	34.723	15.932 (6.933-30.032)	<0.001
Monthly family income (yuan)	0.189	0.763	0.082	0.897 (0.245-2.938)	0.652
Regular prenatal care	-1.836	0.785	6.782	0.782 (0.473-0.892)	0.021
Vegetarian dominated diet	0.923	0.862	1.062	2.217 (0.588-9.873)	0.294
Iron supplementation during pregnancy	-2.482	0.645	5.298	0.673 (0.214-0.892)	0.047
Drinking of strong tea or coffee	1.283	0.972	9.238	1.582 (1.362-2.032)	0.016
Nutritional guidance during pregnancy	-2.081	0.582	7.522	0.815 (0.572-0.941)	0.038

Note: ID: iron deficiency; SE: standard error; OR: odds ratio; CI: confidence interval.

Multivariate logistic regression analysis of ID during pregnancy

Multivariate regression analysis found that age ≥35 years old, number of pregnancies ≥2, number of childbirths >1, number of abortions ≥3 and having strong tea or coffee were risk factors for ID, while regular prenatal cares, iron supplementation and nutritional guidance during pregnancy were protective factors against ID in pregnant women (all P<0.05). See **Tables 2**, **3**.

Risk factors for IDA in pregnant women

IDA developed in 104 of the 721 pregnant women with ID. Univariate analysis found that as compared with the ID group, the IDA group had more subjects with an age over 35 years old, a body mass index less than 18.5 kg/m^2, number of abortions ≥3, a vegetarian dominated diet and a habit of drinking strong tea or coffee, while less with an iron supplementation during pregnancy (P<0.05). See **Table 4**.

Multivariate logistic regression analysis of IDA during pregnancy

Multivariate regression analysis found that age ≥35 years old, number of abortions ≥3 and a habit of drinking strong tea or coffee were risk factors for IDA, while regular prenatal cares and iron supplementation during pregnancy were protective factors against IDA in pregnant women (all P<0.05). See **Tables 5**, **6**.

Comparison of pregnancy outcomes among different groups

The incidences of gestational hypertension, fetal distress, preterm birth, cesarean section, postpartum hemorrhage and neonatal asphyxia in the IDA group were higher than those in the non-ID group (all P<0.05). Also, the incidences of gestational hypertension, cesarean section and postpartum hemorrhage were higher in the IDA group than those in the ID group (all P<0.05). Moreover, the incidences of

Table 4. Potential risk factors for IDA in pregnant women (n, %)

Item	ID group (n=617)	IDA group (n=104)	χ^2/t	P
Age (years)				
≥35	35 (5.67)	30 (28.85)	58.276	<0.001
<35	582 (94.33)	74 (71.15)		
Number of pregnancies				
1	250 (40.52)	49 (47.12)	1.596	0.207
≥2	367 (59.48)	55 (52.88)		
Number of childbirths				
First	252 (40.84)	53 (50.96)	2.652	0.105
>1	365 (59.16)	51 (49.04)		
Body mass index (kg/m^2)				
≥18.5	553 (89.63)	74 (71.15)	26.789	<0.001
<18.5	64 (10.37)	30 (28.85)		
Education level				
High school or above	530 (85.90)	91 (87.50)	0.191	0.662
Below high school	87 (14.10)	13 (12.50)		
Number of abortions				
0	102 (16.53)	17 (16.35)	162.175	<0.001
1-2	471 (76.34)	32 (30.77)		
≥3	44 (7.13)	55 (52.88)		
Monthly family income (yuan)				
≥5000	371 (60.13)	63 (60.58)	0.007	0.931
<5000	246 (39.87)	41 (39.42)		
Regular prenatal care				
Yes	474 (76.82)	48 (46.15)	41.893	<0.001
No	143 (23.18)	56 (53.85)		
Vegetarian dominated diet				
Yes	325 (52.67)	66 (63.46)	4.172	0.041
No	292 (47.33)	38 (36.54)		
Iron supplementation during pregnancy				
Yes	127 (20.58)	10 (9.62)	6.776	0.009
No	490 (79.42)	94 (90.38)		
Drinking of strong tea/coffee				
Yes	141 (22.85)	53 (50.96)	35.755	<0.001
No	476 (77.15)	51 (49.04)		
Nutritional guidance during pregnancy				
Yes	280 (45.38)	52 (50.00)	0.764	0.382
No	337 (54.62)	52 (50.00)		

Note: t is the statistical value of t-test; χ^2 is the statistical value of chi-square test. ID: iron deficiency; IDA: iron deficiency anemia.

gestational hypertension, cesarean section and postpartum hemorrhage in ID group were higher than those in the non-ID group (all P<0.05). See **Table 7**.

Discussion

Anemia is a common disease during pregnancy because the blood volume increase during pregnancy is mainly an increase of plasma, resulting in a limited count of red blood cells and diluted blood. However, the fetus needs iron during its development, so ID and IDA are commonly seen during pregnancy [7]. In this study the incidences of ID and IDA in pregnant women were 59.78% and 8.62%, respectively, which are similar to 48.2% and 13.9% from a survey in 2018 in China [8].

Table 5. Assignment of potential risk factors for IDA in pregnant women

Factor	Independent variable	Assignment
Age (years)	X1	≥35 years old =1, <35 years old =0
Body mass index (kg/m^2)	X2	<18.5=1, ≥18.5=0
Number of abortions	X3	≥3=1, 0-2=0
Regular prenatal care	X4	No=1, Yes=0
Vegetarian dominated diet	X5	Yes=1, No=0
Iron supplementation during pregnancy	X6	No=1, Yes=0
Drinking of strong tea or coffee	X7	Yes=1, No=0

Note: ID: iron deficiency.

Table 6. Potential risk factors for IDA in pregnant women

Factor	β	SE	Wald value	OR value (95% CI)	P
Age (years)	1.622	0.528	10.226	5.253 (1.901-9.233)	0.001
Body mass index (kg/m^2)	0.945	0.719	1.028	2.032 (0.682-8.923)	0.291
Number of abortions	2.734	0.409	34.295	14.923 (7.223-38.912)	<0.001
Regular prenatal care	-1.235	0.923	9.287	0.952 (0.745-0.982)	0.034
Vegetarian dominated diet	0.182	0.734	0.092	0.876 (0.285-2.925)	0.643
Iron supplementation during pregnancy	-1.923	0.745	7.636	0.721 (0.467-0.821)	0.033
Drinking of strong tea or coffee	1.245	0.902	10.221	1.382 (1.124-1.722)	0.029

Note: IDA: iron deficiency anemia; SE: standard error; OR: odds ratio; CI: confidence interval.

Table 7. Comparison of pregnancy outcomes among different groups (n, %)

Group	Gestational hypertension	Fetal distress	Preterm birth	Cesarean section	Postpartum hemorrhage	Neonatal asphyxia
Non-ID group (n=485)	20 (4.12)	22 (4.54)	46 (9.48)	205 (42.27)	19 (3.92)	9 (1.86)
ID group (n=617)	42 (6.81)*	40 (6.48)	78 (12.64)	300 (48.62)*	50 (8.10)*	17 (2.76)
IDA group (n=104)	12 (11.54)*,#	12 (11.54)*	19 (18.27)*	56 (53.85)*,#	10 (9.62)*,#	7 (6.73)*
χ^2	9.163	7.555	7.067	6.864	9.520	7.649
P	0.010	0.023	0.029	0.036	0.009	0.022

Note: Chi-square test was used for comparison among groups. *means comparing with the non-ID group, P<0.05; #means comparing with the ID group, P<0.05. χ^2 is the statistical value of chi-square test. ID: iron deficiency; IDA: iron deficiency anemia.

This study further analyzed the potential risk factors for ID and IDA. We found that the risk factors for ID were age ≥35 years, number of pregnancies ≥2, number of childbirths >1, number of abortions ≥3 and drinking of strong tea or coffee, while the protective factors against ID were regular prenatal cares, iron supplementation and nutrition guidance during pregnancy. The risk factors for IDA were age ≥35 years, number of abortions ≥3 and drinking of strong tea or coffee, while the protective factors against IDA were regular prenatal cares and iron supplementation during pregnancy. Previous studies have shown that the optimal age for female pregnancy is 25-29 years. An age over 30 years can cause undesirable pregnancy outcomes due to decreased body hormone, uterine contractility and elasticity of the birth canal [9, 10]. Another study has shown that the history of pregnancies and induced abortions can cause ID and IDA during the next pregnancy. The reason may be that each pregnancy consumes a large amount of iron in the body. When the iron reserves in the body have not yet been restored after a previous pregnancy or induced abortion, ID and even IDA can be easily developed during the next pregnancy [11]. Besides, a large intake of strong tea or coffee can inhibit the body's absorption of iron and coupled with the consumption of iron during pregnancy this can lead to the occurrence of ID or IDA [12, 13]. Regular prenatal cares are conducive to the early (potential) diagnosis of ID or IDA, and corresponding intervention and pre-

vention can be carried out in time [14]. Pregnant women digest a large amount of iron during pregnancy, so early iron supplementation can effectively prevent the occurrence of ID and IDA. Nutritional dietary guidance can ensure that the nutrition intake during a pregnancy also helps the absorption of iron by supplementing substances such as vitamins [15].

This study showed that both ID and IDA could increase pregnancy related adverse events. The incidences of gestational hypertension, cesarean section and postpartum hemorrhage in the ID group were higher than those in the non-ID group. Also, the incidences of gestational hypertension, fetal distress, preterm birth, cesarean section, postpartum hemorrhage and neonatal asphyxia in the IDA group were all higher than those in the non-ID group. Our results are consistent with those of a previous study [16]. IDA can cause a stress response in pregnant women. Pregnant women with anemia have a decreased ability to carry oxygen in the blood, which increases the cardiovascular and peripheral vascular pressure to meet the need of blood delivery, leading to a risk of hypertension [17]. Blood is an important medium for the delivery of nutrients and oxygen between the mother and the baby. Anemia can decrease those deliveries to the placenta, resulting in an abnormal placental function. For instance, fetal distress can happen due to ischemia, hypoxia and the lack of nutrients, which elevate the risk of preterm birth, cesarean section and neonatal asphyxia [18, 19]. Another study showed that pregnant women with anemia had a reduced synthesis of immune globulin due to an insufficient oxygen supply and lack of nutrients, which decreased their immunity and increased the risk of puerperal infections [20]. Moreover, ID can stimulate the expression of matrix metalloproteinases. Highly expressed matrix metalloproteinases can reduce the uterine contractions and induce postpartum hemorrhage [7]. It can also decrease the uterine contractility because of placental ischemia and hypoxia, leading to postpartum hemorrhage [14].

Limitations and prospects: This is a single-center retrospective study with relatively small sample size, so a multi-center prospective study should be conducted in the future to explore the risk factors for ID and IDA during pregnancy and the impact on pregnancy outcome. Based on the incidence of ID and IDA in plateau area as well as the risk factors, corresponding intervention measures could be formulated for the prevention and treatment of ID and IDA.

To sum up, pregnant women from the plateau region show a high incidence of ID and IDA, especially for the elderly parturient women or those with multiple pregnancies, child births or abortions. To reduce the incidence of ID and IDA as well as to improve pregnancy outcomes, our findings suggest pregnant woman to have regular prenatal care visits and a proper diet by avoiding strong tea or coffee, supplementing iron and receiving nutritional guidance.

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Disclosure of conflict of interest

None.

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