Prevalence of anemia and iron deficiency anemia in Chinese pregnant women (IRON WOMEN): a national cross-sectional survey

CURRENT STATUS: UNDER REVIEW

BMC Pregnancy and Childbirth  BMC Series

Jing Tan
Sichuan University West China Hospital

Guolin He
Sichuan University West China Second University Hospital

Yana Qi
Sichuan University West China Hospital

Hongmei Yang
Sichuan University West China Second University Hospital

Yiquan Xiong
Sichuan University West China Hospital

Chunrong Liu
Sichuan University West China Hospital

Wen Wang
Sichuan University West China Hospital

Kang Zou
Sichuan University West China Hospital

Andy H. Lee
School of Public Health, Curtin University

Xinghui Liu
Sichuan University West China Second University Hospital

Xin Sun
sunx79@hotmail.com Corresponding Author
SUBJECT AREAS
Maternal & Fetal Medicine

KEYWORDS
anemia, iron deficiency anemia, prevalence, risk factors, cross-sectional survey
Abstract
Background: The current evidence about anemia and iron deficiency anemia (IDA) during pregnancy remains elusive in China. The purpose of this study is to investigate the prevalence of anemia and IDA and their risk factors in Chinese pregnant women.
Methods: A nationwide cross-sectional survey of pregnant women was conducted during their antenatal visits. Using a multi-stage sampling method, 24 hospitals from 16 provinces across China were selected. Structured questionnaires were administered to collect information from participants and to extract clinical data from electronic medical records. Mixed-effects logistic regression models were performed to determine the risk factors associated with anemia and IDA.
Results: In total, 12,403 pregnant women were enrolled, including 1,018 (8.2%) at the first trimester, 3,487 (28.1%) at the second, and 7,898 (63.7%) at the third. Overall, 19.8% of women were diagnosed with anemia and 13.9% were diagnosed with IDA. The prevalence of anemia and IDA varied between regions and increased by gestational month, peaking at the eighth gestational month (24.0% for anemia and 17.8% for IDA). Pregnant women at advanced stage of gestation, non-local residents, multiple gestations, multiparity, pre-pregnancy underweight, and those experiencing severe nausea or vomiting during pregnancy, were associated with higher risks of anemia and IDA.
Conclusions: The prevalence of anemia and IDA during pregnancy is high and varies across regions in China, particularly for women at their second and third trimesters. Interventions are needed to improve the condition during pregnancy. Keywords: anemia, iron deficiency anemia, prevalence, risk factors, cross-sectional survey

Introduction
Anemia is the most common pregnancy comorbidity [1, 2], and affects 80% of pregnant women globally [3]. A systematic review of evidence from 107 countries suggested that the prevalence of anemia among pregnant women was 38% (95% CI 33%-43%), impacting approximately 32 million individuals [4], of whom about 75% were manifested with iron deficiency [5]. The prevalence of iron-deficient anemia (IDA), the most common type of anemia, appeared to vary across regions, from 3% in Europe [6] to over 50% in Africa [7, 8].
Anemia and IDA can lead to adverse health outcomes for both mothers and their offspring, including infections, premature rupture of membrane, fetal growth restriction, fetal hypoxia, premature birth, low birth weight and fetal death [9, 10]. In low- and middle-income countries, 12% of low birth weight, 19% of preterm births, and 18% of perinatal mortality, are attributable to maternal anemia [11].

In China, many deliveries take place every year. In 2016, for example, 18,466,561 live births were delivered [12]. In view of the recently implemented two-child policy, reducing anemia and IDA during pregnancy has become a national priority for antenatal care. However, the available prevalence data from a survey (n = 3591) conducted nearly two decades ago [13] were outdated.

In the last decade, China has undergone dramatic social and economic reforms, which have profound impacts on pregnancy care, lifestyles, and maternal and child health. The lack of up-to-date information on the prevalence and risk factors of anemia and IDA has presented a major obstacle for developing evidence-based recommendations for managing pregnant women. To address such an important knowledge gap, we conducted a nationwide cross-sectional survey to investigate the current prevalence of anemia and IDA during pregnancy. Using a hybrid data collection process, the risk factors associated with the development of anemia and IDA for Chinese women were also ascertained in this study.

Methods

Study design

From 19 September to 20 November 2016, a nationwide cross-sectional survey was conducted at 24 hospitals from 16 provinces across China. The hospitals were selected according to the multi-stage sampling method (detailed below). Pregnant women, who attended these hospitals for antenatal care, were consecutively recruited into the study regardless of their gestational stage.

The study was approved by the Research Ethics Committee of West China Second Hospital, Sichuan University (2016-009), and registered at ClinicalTrials.gov (ID number: NCT02887963). All study participants signed an informed consent form. The Department of Obstetrics at West China Second University Hospital and the Chinese Evidence-based Medicine Center at West China Hospital, both from Sichuan University, took the primary responsibilities for study planning and design, project
management, data collection, statistical analysis, and reporting.

**Sampling methods**
We used a multi-stage sampling method for selecting hospitals. According to the classification of the National Bureau of Statistics, the country consisted of six geographic regions (Supplementary Fig. 1).

First, from each region, we selected one teaching hospital as the regional coordinating center.

Subsequently, three cities were randomly selected from that region. Then, from each selected city, we chose one tertiary hospital as a survey site based on our capacity and available resources. In total, 24 tertiary hospitals were included as survey sites (Supplementary Table 1).

The participating hospitals should meet the following criteria: 1) serum ferritin and hemoglobin were routinely tested at the local laboratory; 2) the laboratory facilities were examined by a quality control team comprising senior technicians, and 3) more than 400 pregnant women attending the hospital antenatal clinic during the survey period.

**Patient eligibility**
Our clinical investigators consecutively enrolled eligible pregnant women, regardless of their gestational stage, who were visiting the selected hospitals for antenatal care. Eligibility criteria were: completed an antenatal visit between 19 September and 20 November 2016; agreed to take a blood test and complete the questionnaire survey, by signing an informed consent form. Those pregnant women who had been participating in another clinical study during the same period were excluded.

**Outcome measures**
The primary outcomes were the presence of anemia and IDA. According to the Chinese Guideline for Diagnosis and Treatment of IDA during Pregnancy [14], anemia was diagnosed by hemoglobin less than 110 g/l, and IDA diagnosed by serum ferritin concentration less than 20 µg/l and hemoglobin less than 110 g/l.

All eligible participants were subjected to hemoglobin and serum ferritin examination during their antenatal visit. Blood samples were tested at the local laboratories using standard qualified methods. We also documented previously diagnosed IDA, if available, and when the diagnosis was made (i.e. first, second, or third trimester).

**Data collection**
We used two structured questionnaires which had been pilot tested to collect information. The first questionnaire consisted of items regarding participant demographics, history of pregnancy and childbirth, gestational comorbidities, behavior and lifestyle, previously clinician-diagnosed IDA, and history of other gestational comorbidities. The second clinician-reported questionnaire was completed by manually reviewing electronic medical records (EMRs), including anthropometrics (e.g. height, weight, and abdominal circumference), physical examinations, laboratory results (e.g. hemoglobin, serum ferritin, red blood cell count and leucocyte count), treatment of IDA, and pregnancy complications.

A centralized online electronic data capturing system was set up to collect, review, and store data. Participants either completed the questionnaire through WeChat or webpages, or a hardcopy version which was subsequently uploaded to the central system by trained investigators. Logic verification rules and reference ranges were implemented for data verification.

From each participating woman, we thoroughly collected the following information: demographic characteristics (maternal age, ethnicity, education level, local resident status, registered residential place (urban or rural) and annual family income), gestational characteristics (gestational weeks of pregnancy, multiple gestations, parity, use of assisted reproductive technology (ART), and nausea or vomiting during the first trimester (NVP)), anthropometrics (height, pre-pregnancy weight and current weight), behavior and habits (e.g. active or passive smoking, meat intake), nutrients supplementation (intake of folic acid, multivitamins and calcium supplements), and gestational co-morbidities (e.g. hematological diseases, HBV infection, hypertension, gynecological diseases, diabetes (Type I or Type II), thyroid and autoimmune diseases). Gestational co-morbidities were defined as those conditions diagnosed before conception by clinicians, or diagnoses at the first antenatal visit.

Sample size estimation
Prevalence data reported from a retrospective study was used for the sample size calculation [15]. Assuming a conservative prevalence estimate of maternal IDA being 3.96% (i.e. $p \approx 4\%$), the corresponding $d$ (tolerance error) was taken to be 0.004 (one-tenth of $p$), with $Z_{\alpha/2}=1.96$ and 2-tailed $\alpha=0.05$, the sample size required was $n=9,220$.

Taking into consideration the available study resources and logistics, the investigators decided to increase the sample size to $n=12,000$. Each regional coordinating center planned to enroll at least 800 pregnant women, and the other 18 hospitals were expected to consecutively recruit over 400 participants at each site.

**Statistical analysis**
We summarized and compared baseline characteristics of pregnant women according to gestational stage. Pearson’s chi-square or Fisher’s exact test were applied to categorical variables, and one-way ANOVA or Kruskal-Wallis test to continuous variables. Pre-pregnancy BMI was categorized into underweight ($BMI < 18.5 \text{ kg/m}^2$), normal ($BMI \geq 18.5 \text{ kg/m}^2$ and $< 25 \text{ kg/m}^2$), overweight and obese ($BMI \geq 25 \text{ kg/m}^2$). We included only women with complete data in our analyses.

We compared the observed hemoglobin and serum ferritin levels by study subgroup (singletons; multiple gestations) and by gestational stage (first; second; third trimester), using means and medians when appropriate. Similarly, the frequencies and prevalence of anemia and IDA were compared with respect to trimesters and subgroups of interest.

To determine the pertinent risk factors associated with anemia and IDA, we considered all plausible factors from the literature, namely, demographic characteristics, gestational characteristics, anthropometry indicators, behavior and habits, nutrients supplementation, and gestational co-morbidities; details of these variables were given in the data collection section. Initially, associations with potential factors were explored by fitting univariate logistic regression models accounting for
gestational stage, with significance level set at \( p = 0.1 \). Next, we fitted mixed-effects logistic regression models separately for anemia and IDA. In view of the inherent correlation of observations due to the clustering effects of different hospitals, a mixed-effects logistic regression model with (24) random hospital effects was considered appropriate for our study setting. Finally, we conducted a sensitivity analysis by removing pregnant women with a history of hematological diseases before pregnancy.

**Results**

Using a multi-stage sampling method, 24 hospitals from 21 cities of 16 provinces or municipal cities in China were enrolled in this study (Supplementary Fig. 1). In total, 12,466 eligible pregnant women were invited to participate. After removing 63 refusals, 12,403 participants were included in the analysis (response rate: 99.5%). The number of enrollments varied from 800 to 906 among the regional coordination centers, whereas recruitments were lower in the other hospitals (range: 400 to 443, Supplementary Table 1). The flow chart of the included sample of participants was given in Supplementary Fig. 2.

**Baseline characteristics**

For our sample, 1018 women (8.2%) were at the first trimester, 3487 (28.1%) at the second, and 7898 (63.7%) at the third. Table 1 presents the baseline characteristics of the participants by gestational stage. The mean maternal age was 30 (SD 4) years; with the majority of participants being of Han ethnicity (93.1%), living in urban area (51.5%), attained higher education level (78.8%), and had annual family income over 30 thousand yuan (90.6%) (Table 1). It is evident that pregnant women at the three trimesters differed in a number of baseline characteristics (\( p < 0.05 \)).

| Characteristics | Total (n,%) | First trimester (n,% | Second trimester (n,%) | Third trimester (n,%) | P value |
|-----------------|------------|---------------------|-----------------------|----------------------|---------|
| Number          | 12403 (100.0) | 1018 (8.21) | 3487 (28.11) | 7898 (63.68) | <0.001⁸ |
| Regions         |             |                     |                       |                      |         |
| Southwest       | 2105 (16.97) | 214 (21.02) | 693 (19.87) | 1198 (15.17) |         |
| East            | 2008 (16.19) | 123 (12.08) | 484 (13.88) | 1401 (17.74) |         |
| Central-south   | 2044 (16.48) | 181 (17.78) | 601 (17.24) | 1262 (15.98) |         |
| Northeast       | 2179 (17.57) | 38 (3.73) | 469 (13.45) | 1672 (21.17) |         |
| Northwest       | 2051 (16.54) | 231 (22.69) | 711 (20.39) | 1109 (14.04) |         |
| North           | 2016 (16.25) | 231 (22.69) | 529 (15.17) | 1256 (15.90) | <0.001⁸ |
| Maternal age    |             |                     |                       |                      |         |
| <35 years       | 10595 (85.42) | 893 (87.72) | 2974 (85.29) | 6728 (85.19) |         |
| ≥35 years       | 1808 (14.58) | 125 (12.28) | 513 (14.71) | 1170 (14.81) |         |
|                      | 18–24 (14.58) | 25–34 (12.88) | 35–44 (14.71) | 45+ (14.81) | 0.091 |
|----------------------|---------------|---------------|---------------|-------------|-------|
| Ethnicity            |               |               |               |             |       |
| Han                  | 11542 (93.06) | 959 (94.20)   | 3257 (93.40)  | 7326 (92.76)|       |
| Others               | 861 (6.94)    | 59 (5.80)     | 230 (6.60)    | 572 (7.24)  | 0.1481 |
| Education level      |               |               |               |             |       |
| ≥ 17 years           | 1376 (11.09)  | 120 (11.79)   | 372 (10.67)   | 884 (11.19) |       |
| 13–16 years          | 8403 (67.75)  | 699 (68.66)   | 2306 (66.13)  | 5398 (68.35)|       |
| 10–12 years          | 1698 (13.69)  | 140 (13.75)   | 522 (14.97)   | 1036 (13.12)|       |
| ≤ 9 years            | 926 (7.47)    | 59 (5.80)     | 287 (8.23)    | 580 (7.34)  | 0.021 |
| Local residents      |               |               |               |             |       |
| No                   | 1394 (11.24)  | 120 (11.79)   | 463 (13.28)   | 811 (10.27)|       |
| Yes                  | 11009 (88.76) | 898 (88.21)   | 3024 (86.72)  | 7087 (89.73)| < 0.0011 |
| Registered residential place |       |               |               |             |       |
| Urban                | 6367 (51.33)  | 516 (50.69)   | 1806 (51.79)  | 4045 (51.22)|       |
| Rural                | 6036 (48.67)  | 502 (49.31)   | 1681 (48.21)  | 3853 (48.78)| 0.7761 |
| Annual family income (thousand yuan) |       |               |               |             |       |
| < 30                 | 1167 (9.41)   | 72 (7.07)     | 320 (9.18)    | 775 (9.81)  |       |
| 30–79.9              | 3427 (27.63)  | 263 (25.83)   | 994 (28.51)   | 2170 (27.48)|       |
| 80–119.9             | 3351 (27.02)  | 301 (29.57)   | 1010 (28.96)  | 2040 (25.83)|       |
| 120–199.9            | 2549 (20.55)  | 228 (22.40)   | 686 (19.67)   | 1635 (20.70)|       |
| ≥ 200                | 1909 (15.39)  | 154 (15.13)   | 477 (13.68)   | 1278 (16.18)| < 0.0011 |
| Multiple gestations  |               |               |               |             |       |
| No                   | 12121 (97.84) | 996 (96.70)   | 3372 (98.16)  | 7753 (97.73)|       |
| Yes                  | 282 (2.16)    | 22 (3.30)     | 115 (1.84)    | 145 (2.27)  | < 0.0011 |
| Parity               |               |               |               |             |       |
| Nulliparity          | 8268 (66.66)  | 713 (70.04)   | 2290 (65.67)  | 5265 (66.66)|       |
| Multiparity          | 4135 (33.34)  | 305 (29.96)   | 1197 (34.33)  | 2633 (33.34)| 0.0341 |
| Use of ART           |               |               |               |             |       |
| No                   | 11921 (96.11) | 969 (95.19)   | 3296 (94.52)  | 7656 (96.94)|       |
| Yes                  | 482 (3.89)    | 49 (4.81)     | 191 (5.48)    | 242 (3.06)  | < 0.0011 |
| NVP                  |               |               |               |             |       |
| No                   | 2957 (23.84)  | 167 (16.40)   | 715 (20.50)   | 2075 (26.27)|       |
| Slight               | 7496 (60.44)  | 671 (65.91)   | 2196 (62.98)  | 4629 (58.61)|       |
| Severe               | 1950 (15.72)  | 180 (17.68)   | 576 (16.52)   | 1194 (15.12)| < 0.0011 |
| Pre-pregnancy BMI    |               |               |               |             |       |
| Underweight          | 2147 (17.31)  | 178 (17.49)   | 625 (17.92)   | 1344 (17.02)|       |
| Normal weight        | 8925 (71.96)  | 738 (72.50)   | 2467 (70.75)  | 5720 (72.42)|       |
| Overweight and obese | 1331 (10.73)  | 102 (10.02)   | 395 (11.33)   | 834 (10.56)| 0.4051 |
| Active or passive smoking |       |               |               |             |       |
| No                   | 7710 (57.37)  | 584 (62.46)   | 2178 (62.65)  | 4948 (62.16)|       |
| Yes                  | 4693 (42.63)  | 434 (37.54)   | 1309 (37.35)  | 2950 (37.84)| 0.0041 |
| Meat intake (kg/week): median (lower quartile-upper quartile) | 0.30 (0.15–0.45) | 0.15 (0.10–0.35) | 0.25 (0.10–0.4) | 0.30 (0.15–0.50) | < 0.0012 |
| Intake of folic acid |               |               |               |             |       |
| No                   | 2077 (16.75)  | 181 (17.78)   | 530 (15.20)   | 1366 (17.30)|       |
| Yes                  | 10326 (83.25) | 837 (82.22)   | 2957 (84.80)  | 6532 (82.70)| 0.0141 |
| Intake of multivitamins |       |               |               |             |       |
| No                   | 4305 (34.71)  | 517 (50.79)   | 1322 (37.91)  | 2466 (31.22)|       |
| Yes                  | 8098 (65.29)  | 501 (49.21)   | 2165 (62.09)  | 5432 (68.78)| < 0.0011 |
| Intake of calcium     |               |               |               |             |       |
| No                   | 4367 (35.21)  | 887 (87.13)   | 1664 (47.72)  | 1816 (22.99)|       |
| Yes                  | 8036 (64.79)  | 131 (12.87)   | 1823 (52.28)  | 6082 (77.01)| < 0.0011 |
| Hematological diseases |       |               |               |             |       |
| No                   | 11782 (94.99) | 987 (96.95)   | 3365 (96.50)  | 7430 (94.07)|       |
| Yes                  | 621 (5.01)    | 31 (3.05)     | 122 (3.50)    | 468 (5.93)  | < 0.0011 |
| HBV infection        |               |               |               |             |       |
| No                   | 12097 (97.53) | 999 (98.13)   | 3405 (97.65)  | 7693 (97.40)|       |
| Yes                  | 362 (2.47)    | 10 (0.91)     | 117 (3.05)    | 30 (0.59)   |       |
| Indicator | Sample | Total | First trimester | Second trimester | Third trimester | P value |
|-----------|--------|-------|----------------|------------------|----------------|---------|
| **Hemoglobin: mean (SD)** | All pregnancies | 118.38 (11.52) | 126.78 (10.20) | 118.93 (11.27) | 117.06 (11.32) | < 0.001<sup>1</sup> |
| | Singletons | 118.43 (11.49) | 126.86 (10.23) | 118.99 (11.25) | 117.10 (11.26) | < 0.001<sup>1</sup> |
| | Multiple gestations | 116.47 (12.88) | 123.44 (7.91) | 117.17 (11.73) | 114.86 (13.98) | 0.01<sup>1</sup> |
| **Serum ferritin: median (lower quartile-upper quartile)** | All pregnancies | 20.60 (11.79-36.97) | 54.39 (34.5-54.01) | 28.60 (16.40-50.50) | 16.70 (10.20-27.00) | < 0.001<sup>2</sup> |
| | Singletons | 20.57 (11.7-36.80) | 54.20 (34.37-93.35) | 28.74 (16.40-50.49) | 16.63 (10.20-26.9) | < 0.001<sup>2</sup> |
| | Multiple gestations | 23.65 (13.9-44.44) | 75.7 (35.30-125.6) | 25.0 (13.9-55.25) | 19.7 (12.1-35.00) | < 0.001<sup>2</sup> |

<sup>1</sup>From One-way ANOVA.
<sup>2</sup>From Kruskal-Wallis rank test.

**Hemoglobin and serum ferritin**

Table 2 summarizes the hemoglobin and serum ferritin levels by study subgroups and gestational stage. It appears that both hemoglobin and serum ferritin tended to decrease with advancing trimesters, especially among women with multiple gestations (Table 2).
1407 (17.8%) at the third (Table 3).

Table 3
Frequencies and prevalence of anemia and IDA by gestational stage

| Outcomes          | Sample                  | Total (n, %) | First trimester (n,% | Second trimester (n,% | Third trimester (n,% | P value$^1$ |
|-------------------|-------------------------|-------------|----------------------|----------------------|----------------------|-------------|
| Anemia            | All pregnancies         | 2460 (19.84)| 50 (4.91)            | 577 (16.55)          | 1833 (23.21)         | < 0.001     |
|                   | Singletons              | 2379 (19.63)| 49 (4.92)            | 547 (16.23)          | 1783 (23.00)         | < 0.001     |
|                   | Multiple gestations     | 81 (28.72)  | 1 (4.55)             | 30 (26.09)           | 50 (34.48)           | 0.011       |
| IDA               | All pregnancies         | 1720 (13.87)| 20 (1.96)            | 293 (8.41)           | 1407 (17.82)         | < 0.001     |
|                   | Singletons              | 1662 (13.72)| 19 (1.91)            | 276 (8.19)           | 1367 (17.63)         | < 0.001     |
|                   | Multiple gestations     | 58 (20.57)  | 1 (4.55)             | 17 (14.78)           | 40 (27.59)           | 0.006       |
| Previously diagnosed IDA | All pregnancies | 3796 (30.61)| 53 (5.21)            | 594 (17.03)          | 3149 (39.87)         | < 0.001     |
|                   | Singletons              | 3699 (30.52)| 52 (5.22)            | 564 (16.73)          | 3083 (39.77)         | < 0.001     |
|                   | Multiple gestations     | 97 (34.52)  | 1 (4.55)             | 30 (26.09)           | 66 (45.52)           | < 0.001     |

$^1$From Pearson’s chi-square test.

IDA, iron deficiency anemia.

Compared with singletons, women with multiple gestations experienced higher prevalence of anemia (28.7% vs. 19.6%) and IDA (20.6% vs. 13.7%, Table 3). The prevalence of anemia and IDA increased with gestational stage, and peaked at the eighth month (24.0% for anemia and 17.8% for IDA, Fig. 1).

In addition, 53/1018 (5.2%), 594/3487 (17.0%) and 3149/7898 (39.9%) pregnancies were previously diagnosed with IDA at the three trimesters, respectively (Table 3). The prevalence also increased with the gestational month (Supplementary Fig. 3).

Figure 2 shows that the prevalence of anemia and IDA varied substantially between the six regions of China. The southwest reported the lowest prevalence of anemia (10.0%) and IDA (15.4%), whereas the east area had the highest prevalence in the second trimester (anemia 23.4% and IDA 13.3%), and central-south had the highest prevalence in the third trimester (anemia 35.2% and IDA 28.8%) (Fig. 2).

Risk factors
As shown in Table 4, mixed-effects logistic regression analysis identified the following factors independently associated with a higher risk of anemia: late trimesters, maternal age 35 years or older, non-local residents, multiple gestations, multiparity, pre-pregnancy underweight, severe NVP during early pregnancy, pre-existing IDA and other hematologic diseases. On the other hand, women
who consume multivitamins and more meat were associated with a lower risk of anemia. (Table 4).

The sensitivity analysis by removing pregnant women with hematological diseases diagnosed before pregnancy produced similar results (not presented for brevity).

### Table 4

| Factors                        | Anemia: adjusted OR (95% CI)
|--------------------------------|-------------------------------
| Gestational stage              |                               |
| Second vs. First               | 4.11 (3.02–5.57)              |
| Third vs. First                | 6.10 (4.52–8.22)              |
| Maternal age (≥ 35 vs. <35 years) | 1.22 (1.06–1.40)        |
| Local residents (No vs. Yes)   | 1.18 (1.02–1.36)              |
| Multiple gestations (Yes vs. No) | 1.54 (1.13–2.09)            |
| Parity (Multiparity vs. Nulliparity) | 1.18 (1.06–1.31) |
| Pre-pregnancy BMI              |                               |
| Overweight and obese vs. Normal weight | 0.67 (0.57–0.80) |
| NVP                            |                               |
| Slight vs. No                  | 0.95 (0.93–1.18)              |
| Severe vs. No                  | 1.21 (1.04–1.41)              |
| Intake of multivitamins (Yes vs. No) | 0.58 (0.52–0.65) |
| IDA before pregnancy (Yes vs. No) | 2.92 (2.41–3.54)           |
| Other hematologic diseases (Yes vs. No) | 8.25 (5.19–13.13) |
| Meat intake (kg/week)          | 0.81 (0.68–0.96)              |

1 logistic mixed regression model adjusting for education level, registered residential place, annual family income, use of ART, and intake of folic acid.

2 logistic mixed regression model adjusting for education level, annual family income, intake of folic acid, gynecological diseases, and thyroid diseases.

OR, odds ratio; CI, confidence interval; ART, assisted reproductive technology; NVP, nausea or vomiting during pregnancy; BMI, Body Mass Index.

Similar influencing factors in the same direction of associations were found for IDA, with the exception of maternal age (not significant; Table 4). The sensitivity analysis by removing pregnant women with hematological diseases diagnosed before pregnancy confirmed the same results.

**Discussion**

**Prevalence of anemia and IDA**

Using a large representative sample of pregnant women, we found that 19.8% of Chinese women had anemia and 13.9% had IDA during pregnancy, and the conditions became more prevalent over the progression of gestation. The prevalence of anemia and IDA also varied substantially across geographic regions of China, from the lowest in the southwest to the highest in the central-south.

A recent systematic analysis (2011) reported that the global prevalence of anemia among pregnant women was 38% [16]. In developed countries, the prevalence was lower (for example, anemia: 15.8% in France [17] and 8.8% in U.S [18]; IDA: 16% in Belgian, 3% in Switzerland and 25.7% in Korea [6]).
but the prevalence remained high in developing nations (for example, anemia: 48.2% in Southeast Asia [2] and 53.4% in Congo [8]); IDA: 51.3% in Egypt [7] and 44.5% in Saudi Arabia [19]).

Our findings were similar to those from developed countries. This suggests that pregnancy care for the Chinese population has improved over the past decades. However, due to different diagnostic criteria adopted by studies, one should interpret the findings with caution [20–22]. In China, IDA was defined as anemia plus serum ferritin < 20 µg/l, whereas different thresholds were used in other countries, for example, < 10 µg/l USA [23]; < 15 µg/l Korea [24]; < 12–15 µg/l Europe [6]; and < 30 µg/l Switzerland [25]. Additionally, our study found rapid decline in hemoglobin and serum ferritin levels with advancing gestational stage, consistent with the literatures [6, 26, 27]. The prevalence of anemia and IDA peaked at the eighth gestational month.

**Risk factors for anemia and IDA**

Several risk factors were identified for anemia and IDA. The magnitudes of association for pertinent factors such as advanced trimesters, multiple gestations, IDA prior to pregnancy, and hematological diseases other than IDA, were relatively strong (adjusted odds ratio over 2). The results were consistent with studies on non-Chinese populations [28–31], and have important implications for managing pregnant women with these characteristics who may be at elevated risk. The sensitivity analysis by excluding those with previously diagnosed IDA or anemia have further confirmed the apparent adverse effect of these factors on the development of anemia or IDA.

In addition, several other factors were found to be moderately associated with the prevalence of anemia and IDA (adjusted odds ratios between 1.2 and 1.3), including non-local residents, multiparity, severe NVP, and pre-pregnancy underweight, similar to findings reported in the literature [24, 31–36]. These factors should also be taken into account when planning for interventions to improve the anemia and IDA status of Chinese pregnant women.

**Supplementation and screening**

Multivitamins supplement and meat intake were associated with lower risk of anemia and IDA. Multivitamins products, which contain vitamins and minerals including iron [37, 38], are commonly consumed in China. The finding concerning meat intake was consistent with previous studies in
Ethiopia [25, 39, 40], in which IDA was found more prevalent in regions with iron-poor diets such as central south, northwest, and east China [24, 41].

Prophylactic iron supplementation for pregnant women is a controversial issue [20–22]. Although the current Chinese guideline does not recommend such supplementation [14], our findings suggest that iron supplements and dietary improvement may be warranted for susceptible and high-risk population subgroups. It has been recommended that all pregnant women should be screened for anemia during pregnancy [3, 23, 42]. However, the timing of screening remains uncertain. At present, the Chinese guideline recommends screening of hemoglobin at the first antenatal visit, with repeated screening every 8–10 weeks [14]. Our result supports such screening, especially at the advanced stage of gestation.

Strengths and limitations
Our study has several advantages. In this nationwide survey, a multi-stage sampling method was applied to select the data collection sites. To our knowledge, this was the largest study ever undertaken in China to investigate the prevalence and risk factors of anemia and IDA during pregnancy. Moreover, rigorous methods were adopted for data collection, ensuring high quality information obtained across the country with minimal missing values. The large sample size has enabled the estimation of overall prevalence of anemia and IDA, as well as facilitated the comparison of rates between regions, population subgroups, and across gestational stage.

Several limitations should be taken into consideration. Firstly, due to logistics problem, hemoglobin and serum ferritin were tested at local laboratories, where the diagnostic accuracy may vary slightly. To circumvent the problem, each participating tertiary hospital was required to be equipped with qualified facilities and professional technicians, and a laboratory quality control team was set up to minimize measurement errors, thus ensuring the reliability and comparability of results. Secondly, random sampling for hospital selection was not feasible due to the vastness of regions and economic constraints. We chose this approach to optimize the balance between available resource and the representativeness of our study locations. Thirdly, all the participating data collection sites were tertiary hospitals with laboratory facilities, the generalizability of findings may be slightly
compromised without the inclusion of smaller hospitals and community clinics.

**Conclusion**

The prevalence of anemia and IDA among Chinese pregnant women remains high, particularly for those at their third trimester of gestation, which peak at the eighth gestational month. Non-local residents, multiple gestations, multiparity, pre-pregnancy underweight, severe NVP, hematologic diseases before pregnancy and other hematologic diseases rather than IDA were associated with higher risks of anemia and IDA. Our study highlights the need for developing and implementing a rigorous management plan to control pregnancy anemia and IDA in China.

**Abbreviations**

IDA, iron deficiency anemia; EMR, electronic medical records; ART, assisted reproductive technology; NVP, nausea or vomiting during pregnancy; HBV, hepatitis B viral; BMI, body mass index; aOR, adjusted Odds Ratio; CI, confidence interval

**Declarations**

**Acknowledgments**

Steering Committee: Xing-hui Liu, Xin Sun, Jing He, Li Zou, Caixia Liu, Yinli Cao, Ling Fan, Xu Chen, Guo-lin He and Jing Tan

Methods Coordination Center: Xin Sun, Jing Tan, Xing-hui Liu, Ya-na Qi and Kang Zou

List of investigators from 24 hospitals: West China Second Hospital, Sichuan University (Xinghui Liu, Guolin He, Lingling Peng & Hongmei Yang); Sichuan Provincial Hospital for Women and Children (Yan Gao), Panzhihua Central Hospital (Xiuli Liu); Chongqing Health Center for Women and Children (Wei Zhou), Women’s Hospital School of Medicine, Zhejiang University (Jing He & Lu Chen); Xiamen Medical Center for Women and Children (Xueqin Zhang); Wenzhou People's Hospital (Hongping Zhang); Suzhou Second People's Hospital/ Suzhou Municipal Hospital (Yun Wang & Xiufen Xu); Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (Li Zou); Maternal and Child Health Hospital of Hubei Province (Mei Xiao & Min Peng); The First Affiliated Hospital of Zhengzhou University (Xianlan Zhao & Yan Zhou); The First Affiliated Hospital of Guangxi Medical University (Hui
Tang); Shengjing Hospital of China Medical University (Caixia Liu & Chong Qiao); Maternal and Child Health Hospital of Dalian (Fang Zhan); Changchun Obstetrics-Gynecology Hospital (Chunxia Yin); The Fourth Affiliated Hospital of Harbin Medical University (Yan Cai); Shanxi Provincial Hospital for Women and Children/ Northwest Women’s and Children’s Hospital (Yinli Cao); The Second Affiliated Hospital of Shanxi University of Traditional Chinese Medicine (Ningxia Yuan); Yan’an University Affiliated Hospital (Hongmei Li); Maternal and Child Health Hospital of Urumchi, Xinjiang (Guifeng Ding & Yan Peng); Beijing Obstetrics and Gynecology Hospital, Capital Medical University (Ling Fan & Jieyan Li); Tianjin Central Hospital of Gynecology Obstetrics (Xu Chen); The Fourth Hospital of Shijiazhuang/ Shijiazhuang Obstetrics and Gynecology Hospital (Guohua Zhang); and Beijing Friendship Hospital, Capital Medical University (Jiewen Zhang), for their efforts for participants enrollment and data collection.

Authors’ contributions

Study conceptualization and design: Xinghui Liu, Xin Sun, and Jing Tan. Study management and oversight: Xinghui Liu, Jing Tan, Guolin He, Yana Qi and Hongmei Yang. Data analysis: Jing Tan and Wen Wang. Draft of the manuscript: Jing Tan. Critical revision: Andy Lee, Xin Sun, Yana Qi, Yiquan Xiong, Chunrong Liu and Kang Zou. All the authors have reached agreement on the results and conclusion and approved the final version of the manuscript.

Funding

This study was funded by The National Natural Science Foundation of China (No. 71704122, 81590955), The National Key Research and Development Program of Reproductive Health & Major Birth Defects Control and Prevention (No.2016YFC1000406), The National Science and Technology Major Project (No. 2018ZX10302206), The National Key Development Plan for Precision Medicine Research (No. 2017YFC0910004), and “Thousand Youth Talents Plan” of China (No. D1024002).

Availability of data and materials
Data of the present research is available by contacting the corresponding author on reasonable request.

**Ethics approval and consent to participate**

The study was approved by the Research Ethics Committee of West China Second Hospital, Sichuan University (2016-009), and each participant should sign an informed consent form.

**Consent for publication**

Not applicable.

**Conflict of Interest**

The authors declare that they have no conflict of interest.

**References**

1. Goonewardene M, Shehata M, Hamad A. Anaemia in pregnancy. Best practice & research Clinical obstetrics & gynaecology. 2012;26:3-24. 10.1016/j.bpobgyn.2011.10.010
2. World Health Organization. In de Benoist B, Mclean E, Egli I & Cogswell M (eds.). Worldwide prevalence of anaemia 1993-2005. WHO Global Database on Anaemia Geneva: World Health Organization, 2008 (NLM: WH 155).
3. Centers for Disease Control and Prevention (CDC). Recommendations to prevent and control iron deficiency in the United States. MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports. 1998;47:1-29.
4. Stevens GA, Finucane MM, De-Regil LM, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of
population-representative data. The Lancet Global health. 2013;1:e16-25.
10.1016/s2214-109x(13)70001-9

5. International Nutritional Anemia Consultative Group (INACG) WHO, United Nations Childrens Fund (UNICEF). Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia. Stoltzfus RJ, ML D, editors. Washington DC, USA: ILSI Press; 1998.

6. Nils Milman CLT, Joyce Merkel, Patsy M Brannon. Iron status in pregnant women and women of reproductive age in Europe. The American journal of clinical nutrition. 2017;106(Suppl). 10.3945/ajcn

7. Rezk M, Marawan H, Dawood R, et al. Prevalence and risk factors of iron-deficiency anaemia among pregnant women in rural districts of Menoufia governorate, Egypt. Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology. 2015;35:663-6. 10.3109/01443615.2014.991289

8. Tandu-Umba B, Mbangama AM. Association of maternal anemia with other risk factors in occurrence of Great obstetrical syndromes at university clinics, Kinshasa, DR Congo. BMC Pregnancy Childbirth. 2015;15:183. 10.1186/s12884-015-0623-z

9. Haider BA, Olofin I, Wang M, et al. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. Bmj. 2013;346:f3443. 10.1136/bmj.f3443

10. Iqbal S, Ekmekcioglu C. Maternal and neonatal outcomes related to iron supplementation or iron status: a summary of meta-analyses. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2017:1-13.
10.1080/14767058.2017.1406915
11. Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. The American journal of clinical nutrition. 2016;103:495-504. 10.3945/ajcn.115.107896

12. National Health and Family Planning Commission. China Health and Family Planning Statistical Yearbook (2017). http://www.yearbookchina.com/navibooklist-N2017120225-1.html 2017

13. Liao QK, Chinese Children, Pregnant Women & Premenopausal Women Iron Deficiency Epidemiological Survey Group. Prevalence of iron deficiency in pregnant and premenopausal women in China: A nationwide epidemiological survey. Chin J Hematol. 2004;25:653-57.

14. Society of Perinatal Medicine, Chinese Medical Association. Guideline for diagnosis and treatment of iron deficiency and iron deficiency anemia in pregnancy. Chin J Perinat Med. 2014;17:451-54.

15. Tan J, Liu XH, Yu C, et al. Effects of medical co-morbidities on severe maternal morbidities in China: a multicenter clinic register study. Acta obstetricia et gynecologica Scandinavica. 2015;94:861-8. 10.1111/aogs.12657

16. Stevens GA, Finucane MM, De-Regil LM, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. The Lancet Global Health. 2013;1:e16-e25. 10.1016/s2214-109x(13)70001-9

17. Thierry Harvey AZ, Marie Auges, Thierry Clavel. Assessment of iron deficiency and anemia in pregnant women: an observational French study. Womens Health. 2015.

18. Le CH. The Prevalence of Anemia and Moderate-Severe Anemia in the US Population
(NHANES 2003-2012). PloS one. 2016;11:e0166635. 10.1371/journal.pone.0166635

19. Baradwan S, Alyousef A, Turkistani A. Associations between iron deficiency anemia and clinical features among pregnant women: a prospective cohort study. Journal of blood medicine. 2018;9:163-9. 10.2147/JBM.S175267

20. Pavord S, Myers B, Robinson S, et al. UK guidelines on the management of iron deficiency in pregnancy. British journal of haematology. 2012;156:588-600.

21. World Health Organization. Guideline: Daily iron and folic acid supplementation in pregnant women. 2012.

22. Peyrin-Biroulet L WN, Cacoub P. Guidelines on the diagnosis and treatment of iron deficiency across indications: a systematic review. The American journal of clinical nutrition. 2015;102:1585-94.

23. ACOG Practice Bulletin No. 95: anemia in pregnancy. Obstetrics and gynecology. 2008;112:201-7. 10.1097/AOG.0b013e3181809c0d

24. Lee JO, Lee JH, Ahn S, et al. Prevalence and risk factors for iron deficiency anemia in the korean population: results of the fifth KoreaNational Health and Nutrition Examination Survey. Journal of Korean medical science. 2014;29:224-9. 10.3346/jkms.2014.29.2.224

25. Abay A, Yalew HW, Tariku A, et al. Determinants of prenatal anemia in Ethiopia. Archives of public health = Archives belges de sante publique. 2017;75:51. 10.1186/s13690-017-0215-7

26. Bah A, Pasricha SR, Jallow MW, et al. Serum Hepcidin Concentrations Decline during Pregnancy and May Identify Iron Deficiency: Analysis of a Longitudinal Pregnancy Cohort in The Gambia. The Journal of nutrition. 2017;147:1131-7. 10.3945/jn.116.245373

27. van Santen S, Kroot JJ, Zijderveld G, et al. The iron regulatory hormone hepcidin is
decreased in pregnancy: a prospective longitudinal study. Clinical chemistry and laboratory medicine. 2013;51:1395-401. 10.1515/cclm-2012-0576

28. Sukrat B, Suwathanapisate P, Siritawee S, et al. The prevalence of iron deficiency anemia in pregnant women in Nakhonsawan, Thailand. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2010;93:765-70.

29. Gebreweld A, Tsegaye A. Prevalence and Factors Associated with Anemia among Pregnant Women Attending Antenatal Clinic at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia. Advances in hematology. 2018;2018:3942301. 10.1155/2018/3942301

30. Ru Y, Pressman EK, Cooper EM, et al. Iron deficiency and anemia are prevalent in women with multiple gestations. The American journal of clinical nutrition. 2016;104:1052-60. 10.3945/ajcn.115.126284

31. Karaoglu L, Pehlivan E, Egri M, et al. The prevalence of nutritional anemia in pregnancy in an east Anatolian province, Turkey. BMC Public Health. 2010;10:329. 10.1186/1471-2458-10-329

32. Mocking M, Savitri AI, Uiterwaal C, et al. Does body mass index early in pregnancy influence the risk of maternal anaemia? An observational study in Indonesian and Ghanaian women. 2018;18:873. 10.1186/s12889-018-5704-2

33. Tan J, Qi YN, He GL, et al. Association between Maternal Weight Indicators and Iron Deficiency Anemia during Pregnancy: A Cohort Study. Chinese medical journal. 2018;131:2566-74. 10.4103/0366-6999.244109

34. Baig-Ansari N, Badruddin SH, Karmaliani R, et al. Anemia prevalence and risk factors in pregnant women in an urban area of Pakistan. Food Nutr Bull. 2008;29:132-9. 10.1177/156482650802900207

35. Bencaiova G, Burkhardt T, Breymann C. Anemia-prevalence and risk factors in
pregnancy. European journal of internal medicine. 2012;23:529-33. 10.1016/j.ejim.2012.04.008

36. Fiaschi L, Nelson-Piercy C, Gibson J, et al. Adverse Maternal and Birth Outcomes in Women Admitted to Hospital for Hyperemesis Gravidarum: a Population-Based Cohort Study. Paediatric and perinatal epidemiology. 2018;32:40-51. 10.1111/ppe.12416

37. Ning M, Chen Y, Zheng Q, et al. Insignificant interference of Elevit in pregnant women serum samples with HBsAg immunoassay on Sysmex. J Clin Lab Anal. 2018:e22725. 10.1002/jcla.22725

38. Diemert A, Lezius S, Pagenkemper M, et al. Maternal nutrition, inadequate gestational weight gain and birth weight: results from a prospective birth cohort. BMC pregnancy and childbirth. 2016;16:224. 10.1186/s12884-016-1012-y

39. Weldekidan F, Kote M, Girma M, et al. Determinants of Anemia among Pregnant Women Attending Antenatal Clinic in Public Health Facilities at Durame Town: Unmatched Case Control Study. Anemia. 2018;2018:8938307. 10.1155/2018/8938307

40. Obse N, Mossie A, Gobena T. Magnitude of anemia and associated risk factors among pregnant women attending antenatal care in Shalla Woreda, West Arsi Zone, Oromia Region, Ethiopia. Ethiopian journal of health sciences. 2013;23:165-73.

41. Zimmermann MB, Hurrell RF. Nutritional iron deficiency. Lancet (London, England). 2007;370:511-20. 10.1016/s0140-6736(07)61235-5

42. Department of Veteran Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Management of Pregnancy. http://www.healthquality.va.gov/guidelines/WH/up/. 2009

Figures
Figure 1

Prevalence of anemia and iron deficiency anemia by gestational month.
Figure 2

Prevalence of anemia and iron deficiency anemia by gestational stage and region.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

Supplementation.docx