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RESEARCH ARTICLE

Prevalence of anemia of varying severity, geographic variations, and association with metabolic factors among women of reproductive age in China: a nationwide, population-based study

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Abstract **To investigate the epidemiological characteristics of anemia of varying severity among women of reproductive age, we conducted a nationwide, cross-sectional study between January 1, 2019 and December 31, 2019, including 4 184 547 nonpregnant women aged 18–49 years from all 31 provinces in the mainland of China. Anemia was defined as having hemoglobin concentration < 120.0 g/L and categorized as mild, moderate, and severe. Multivariate logistic models with cluster effect were used to explore the association of anemia and metabolic risk factors. The standardized prevalence of anemia and moderate and worse anemia among women of reproductive age in China was 15.8% (95% CI 15.1%–16.6%) and 6.6% (6.3%–7.0%), respectively. The prevalence of anemia and the proportion of moderate and worse anemia significantly increased with age. We also observed great geographic variations in the prevalence of anemia, with a high likelihood in south, central, and northwest China. Moderate and/or severe anemia was positively associated with overweight and obesity, diabetes, and impaired kidney function. In conclusion, anemia remains a significant challenge for women of reproductive age in China. Geographic variations and metabolic risk factors should be considered in the comprehensive and targeting strategy for anemia reduction.**

Keywords anemia; prevalence; women of reproductive age; metabolic factor; body mass index; China

Introduction

Anemia continues to be a global public health problem. In particular, approximately 571 million women worldwide are suffering an increased risk of poor health, illness, death, adverse pregnancy outcomes, and weak growth and development due to anemia [1]. Between 1990 and 2021, the global anemia prevalence had a lower decline in women than in men [2]. Although the world health goal proposes reducing the anemia prevalence by 50% among reproductive women by 2025 compared with the 1993–2005 baseline level [3], the prevalence rose from 28.5% in 2013 to 29.9% in 2019 [4].

Anemia is a consequence of multiple conditions and diseases, with the most common causes as nutrient deficiency, chronic infection, and inherited blood disorders (e.g., thalassemia and sickle cell anemia) [1].

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Along with the rapid change in dietary structure and lifestyle, nutritional imbalance (e.g., high-energy and -fat diet and insufficient intake of fruits and vegetables) and related metabolic disorders are spreading in the population, which are recognized as important causes of anemia, such as folic acid and vitamin B12 deficiency, overweight, and obesity [5]. The contribution of these risk factors to the anemia prevalence varies by population, age, and geographic variations. The World Health Organization (WHO) proposes further research on the etiology of anemia and targeted interventions to accelerate the reduction of anemia [1].

In China, the prevalence of anemia of varying severity differs in demographic characteristics and geographic regions, but this variation has not been fully explored [6–8]. Specifically, women of reproductive age have been facing an increasing risk of anemia since 2010 [4]. The prevalence of overweight and obesity is rapidly increasing in the population [9]. However, few studies focus on the association between anemia and metabolic disorders among women of reproductive age. Additional evidence on the epidemiological characteristics in anemia is needed to design and implement a comprehensive and targeted intervention strategy in China.

The primary purpose of this study was to estimate the prevalence of anemia of varying severity among women of reproductive age and reveal the geographic variations in China. The second purpose was to explore the potential association of anemia of varying severity and metabolic risk factors, particularly overweight and obesity, to provide risk stratification of anemia for a comprehensive and targeted strategy for anemia prevention and management.

Materials and methods

Participants and study design

This work was a nationwide, cross-sectional study in the mainland of China before the COVID-19 pandemic. We used individual-based data in the Meinian Healthcare Group system from 231 prefecture-level cities of all 31 provinces between January 1, 2019 and December 31, 2019. The details of the health screening system have been reported in previous studies [10]. Participants in the system were mainly local employees and residents in urban areas and received health check-up services in local screening centers. The system had established a unified quality control flow for data collection of demographic information, body measurement, and biochemical detection. Vein blood samples were collected for each eligible participant to measure hemoglobin (Hb) concentration. We included nonpregnant women of reproductive age (18–49 years) in this study.

Primary outcome and explanatory variables

Referring to the definition of anemia among nonpregnant women aged 15 years and over from the WHO guideline and the American Society of Hematology [4,11,12], we defined anemia as having Hb concentration < 120.0 g/L. We adjusted the Hb concentration by the average altitude of prefecture-level cities on the basis of WHO's recommendation (Appendix 1 in supplementary material) [7]. Furthermore, anemia was categorized as mild (Hb of 110.0–119.9 g/L), moderate (Hb of 80.0–109.9 g/L), and severe (< 80.0 g/L). Moderate and severe anemia were further combined into moderate and worse (< 110.0 g/L) to show the severity of anemia.

We included several explanatory variables, including (1) age group by 5 years (18–24, 25–29, 30–34, 35–39, 40–44, and 45–49 years); (2) geographic regions (north, east, central, south, southwest, northeast, and northwest); (3) body mass index (BMI), divided into underweight (< 18.5 kg/m^2), normal (18.5–23.9 kg/m^2), and overweight/obese (⩾ 24 kg/m^2); (4) other metabolic factors, including hypertension (defined as systolic pressure ⩾ 140 mmHg and/or diastolic pressure ⩾ 90 mmHg), diabetes (defined as fasting glucose ⩾ 7.0 mmol/L), high total cholesterol (TC, defined as TC ⩾ 5.2 mmol/L), high triglyceride (TG, defined as TG ⩾ 1.7 mmol/L), hyperuricemia (defined as blood uric acid ⩾ 360 μmol/L), and impaired kidney function (IKF, defined as estimated glomerular filtration rate < 60 mL/min per 1.73 m^2 on the basis of serum creatinine using the chronic kidney disease epidemiology collaboration 2009 equation); (5) history of cesarean delivery. Additionally, we adjusted for city-level per capita gross domestic product (GDP) in 2018, province-level unemployment rate, and province-level proportion of college education or above among the population aged 20 years and above.

Statistical analyses

We described the characteristics of overall participants and anemic patients of varying severity and compared the distribution of covariates between normal and anemic women. Continuous variables were summarized as means (SD), and categorical variables as frequencies and proportions. We separately estimated the prevalence of anemia, subtype anemia of different severity, and moderate and worse anemia overall and by covariates. The percentages and prevalence were standardized using combined weighted coefficients. Weighted coefficients accommodated the population size at the province level and the poststratification weights, which harmonized the sample structure of the study with that of the 2020 national census of the Chinese population [13]. Variances and 95% confidence interval (CI) were estimated by the Taylor series linearization considering the cluster effect of cities. Differences between groups were tested using the Kruskal–Wallis *t*-test or χ^2 test with Rao–Scott correction.

Furthermore, we estimated the provincial prevalence of anemia of varying severity. If the 95% CI was more than 30% of the prevalence estimate, the bootstrap estimation with 1000 iterations would be used [14]. We compared the prevalence among seven geographic regions and fitted logistic models to show geographic variations. To explain the variations, we conducted various ecological analyses. We calculated the urbanization rate and the proportion of four food groups at the province level, including the meat, fish, and egg group, the vegetable and fruit group, cereal, and sugar, on the basis of *China Statistical Yearbook 2018* [15]. Then, linear regression was performed for the correlation between the standardized prevalence of provincial anemia and urbanization and the proportion of four food groups.

We fitted multivariable logistic regression for anemia of varying severity, taking normal women as a reference. The fixed effects of explanatory variables were used to estimate odds ratios (ORs), and 95% CIs were estimated using robust SEs clustered by city, adjusting for regional covariates. To further explore the association between BMI and anemia of varying severity, BMI was fitted as a four-knot restricted cubic spline at the 5th, 35th, 65th, and 95th percentiles to allow for nonlinearity. We also fitted models on data without missing values and added interaction terms between age and other factors as sensitivity analyses.

With the assumption of missing data following multiple normal distributions, we applied a multiple imputation for BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), blood uric acid (UA), and serum creatinine based on Markov chain Monte Carlo. All missing values were imputed 10 times, and the average imputations were used for analysis (Appendix 2 in supplementary material).

All statistical tests were two-sided; a *P* value less than 0.05 was considered statistically significant. Considering that a large sample size may increase the probability of statistical differences, we referred to Benjamin and colleagues' suggestion (raise the significance threshold, e.g., $P < 0.005$) and provided exact *P* values of 0.0001 or larger to facilitate the interpretation [16]. All analyses were conducted with SAS 9.4 or R packages (3.5.1).

Results

Characteristics of participants

Between January 1, 2019 and December 31, 2019, 4 638 827 nonpregnant women aged 18–49 years participated in a health examination, of whom 454 280 were excluded because of missing values for Hb concentration or all demographic and metabolic factors (9.8%; Fig. S1). Finally, 4 184 547 eligible women were included in analyses, and the difference between included and excluded women is presented in Table S1.

Table 1 presents the characteristics of the participants in the study. The mean age was 35.4 years (SD 8.3). A total of 661 927 women were diagnosed with anemia, of which 41.5% were moderate and worse. The proportion of obesity, hypertension, diabetes, high TC, high TG, hyperuricemia, and IKF was 22.5%, 7.0%, 1.2%, 20.9%, 12.3%, 8.1%, and 0.1%, respectively. No significant differences existed between crude and standardized results (Table S2). Compared with normal women, anemic women were less likely to be overweight or obesity or to have hypertension, diabetes, high TC, high TG, or hyperuricemia and were more likely to have IKF

Table 1 Characteristics of participants and anemic patients stratified by severity

	Overall	Unanemic	Anemic	Severity of anemia			
				Mild	Moderate	Severe	Moderate and worse
N	4 184 547	3 522 620	661 927	386 818	256 498	18 610	275 108
Age (years)	35.4±8.3	35.1±8.3	37.0±7.8	36.2±7.9	38.0±7.6	40.4±7.1	38.2±7.6
Age group							
18–24	507 447 (12.1)	454 248 (12.9)	53 199 (8.0)	35 981 (9.3)	16 500 (6.4)	718 (3.9)	17 218(6.3)
25–29	631 059 (15.1)	559 515 (15.9)	71 544 (10.8)	48 191 (12.5)	22 424 (8.7)	929 (5.0)	23 353(8.5)
30–34	877 056 (21.0)	747 429 (21.2)	129 627 (19.6)	82 468 (21.3)	44 955 (17.5)	2203 (11.8)	47 159(17.1)
35–39	699 362 (16.7)	570 795 (16.2)	128 566 (19.4)	74 387 (19.2)	50 897 (19.8)	3282 (17.6)	54 179(19.7)
40–44	657 574 (15.7)	526 232 (14.9)	131 341 (19.8)	69 974 (18.1)	56 657 (22.1)	4710 (25.3)	61 367(22.3)
45–49	812 050 (19.4)	664 401 (18.9)	147 649 (22.3)	75 817 (19.6)	65 064 (25.4)	6768 (36.4)	71 832(26.1)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Body mass index							
< 18.5	325 585 (7.8)	279 377 (7.9)	46 208 (7.0)	30 548 (7.9)	14 964 (5.8)	696 (3.7)	15 660 (5.7)

(*Continued*)

	Overall	Unanemic	Anemic	Severity of anemia			
				Mild	Moderate	Severe	Moderate and worse
18.5–23.9	2 629 606 (62.8)	2 200 595 (62.5)	429 011 (64.8)	256 683 (66.4)	161 230 (62.9)	11 098 (59.6)	172 328 (62.6)
24.0–27.9	941 997 (22.5)	794 540 (22.6)	147 456 (22.3)	79 044 (20.4)	63 098 (24.6)	5314 (28.6)	68 412 (24.9)
⩾ 28.0	287 360 (6.9)	248 108 (7.0)	39 251 (5.9)	20 542 (5.3)	17 206 (6.7)	1502 (8.1)	18 709 (6.8)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Hypertension							
No	3 890 797 (93.0)	3 273 408 (92.9)	617 389 (93.3)	364 324 (94.2)	235 937 (92.0)	17 129 (92.0)	253 065 (92.0)
Yes	293 750 (7.0)	249 212 (7.1)	42 077 (6.7)	22 495 (5.8)	20 562 (8.0)	1482 (8.0)	22 043 (8.0)
P value	NA	NA	0.0008	< 0.0001	< 0.0001	0.0002	< 0.0001
Diabetes							
No	4 132 727 (98.8)	3 476 836 (98.7)	655 892 (99.1)	383 811 (99.2)	253 744 (98.9)	18 336 (98.5)	272 080 (98.9)
Yes	51 820 (1.2)	45 784 (1.3)	6035 (0.9)	3007 (0.8)	2754 (1.1)	274 (1.5)	3028 (1.1)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	0.08	< 0.0001
High total cholesterol							
No	3 308 125 (79.1)	2747 138 (78.0)	560 986 (84.8)	322 625 (83.4)	220 668 (86.0)	17 693 (95.1)	238 361 (86.6)
Yes	876 422 (20.9)	775 482 (22.0)	100 941 (15.2)	64 193 (16.6)	35 830 (14.0)	917 (4.9)	36 747 (13.4)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
High triglyceride							
No	3 668 817 (87.7)	3070 575 (87.2)	598 242 (90.4)	350 161 (90.5)	231 086 (90.1)	16 995 (91.3)	248 081(90.2)
Yes	515 730 (12.3)	452 045 (12.8)	63 685 (9.6)	36 657 (9.5)	25 412 (9.9)	1615 (8.7)	27 028 (9.8)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Hyperuricemia							
No	3 843 648 (91.9)	3213 550 (91.2)	630 098 (95.2)	365 676 (94.5)	246 350 (96.0)	18 071 (97.1)	264 421(96.1)
Yes	340 899 (8.1)	309 070 (8.8)	31 829 (4.8)	21 142 (5.5)	10 148 (4.0)	539 (2.9)	10 687 (3.9)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Impaired kidney function							
No	4 179 685 (99.9)	3519 307 (99.9)	660 378 (99.8)	385 810 (99.7)	256 017 (99.8)	18551(99.7)	274 568(99.8)
Yes	4 862 (0.1)	3314 (0.1)	1549 (0.2)	1008 (0.3)	481 (0.2)	59 (0.3)	540 (0.2)
P value	NA	NA	< 0.0001	0.0009	< 0.0001	< 0.0001	0.0025
History of cesarean delivery							
No	3931 813 (94.0)	3316 126 (94.1)	615 686 (93.0)	360 436 (93.2)	238 041 (92.8)	17 209 (92.5)	255 250 (92.8)
Yes	252 735 (6.0)	206 494 (5.9)	46 241 (7.0)	26 382 (6.8)	18 457 (7.2)	1401 (7.5)	19 859 (7.2)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Geographic region							
North	533 236 (12.7)	451 438 (12.8)	81 798 (12.4)	43 399 (11.2)	35 886 (14.0)	2513 (13.5)	38 399 (14.0)
East	1 327 314 (31.7)	1 114 428 (31.6)	212 886 (32.2)	122 880 (31.8)	83 681 (32.6)	6325 (34.0)	90 006 (32.7)
Central	610 892 (14.6)	507 817 (14.4)	103 076 (15.6)	61 152 (15.8)	38 971 (15.2)	2953 (15.9)	41 924 (15.2)
South	566 412 (13.5)	466 625 (13.3)	99 787 (15.1)	62 160 (16.1)	35 555 (13.9)	2071 (11.1)	37 626 (13.7)
Southwest	544 950 (13.0)	480 102 (13.6)	64 848 (9.8)	39 937 (10.3)	23 278 (9.1)	1633 (8.8)	24 911 (9.1)
Northwest	282 513 (6.8)	234 518 (6.7)	47 995 (7.3)	26 031 (6.7)	20 104 (7.8)	1860 (10.0)	21 964 (8.0)
Northeast	319 230 (7.6)	267 693 (7.6)	51 538 (7.8)	31 260 (8.1)	19 023 (7.4)	1255 (6.7)	20 278 (7.4)
P value	NA	NA	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001

P values were statistically tested for characteristics between anemic and unanemic women. Continuous variables were presented with mean ± standard deviation and categorical variables with number and proportion. Abbreviations: NA, not applicable.

and a history of cesarean delivery and to reside in central, south, and northeast China. Stratified by severity, women with mild anemia were less likely to be overweight or obesity and to have hypertension or diabetes. Those with moderate anemia were more likely to be overweight and have hypertension, while those with severe anemia were more likely to be overweight or obesity and to have hypertension and diabetes.

Epidemiological pattern of anemia among women of reproductive age

The standardized prevalence of overall, mild, moderate, severe, and moderate and worse anemia in Chinese women of reproductive age was estimated as 15.8% (95% CI 15.1%–16.6%), 9.2% (8.8%–9.7%), 6.1% (5.8%–6.5%), 0.4% (0.4%–0.5%), and 6.6% (6.3%–7.0%), respectively, which accorded with crude estimates (Tables 2 and S3). The age-specific prevalence of anemia rose significantly with age, reaching the highest at 40–44 years (Fig. 1). The rising trend was more obvious for moderate and severe anemia than for mild anemia. Accordingly, the proportion of moderate and severe anemia gradually increased with age.

Figure 2 shows the geographic variations in the prevalence of anemia of varying severity among women by age groups (Tables S4–S6). The highest standardized prevalence of anemia was observed in Xizang (25.1%, 95% CI 24.1%–26.3%), showing 2.6-fold differences compared with the lowest prevalence in Guizhou (9.3%, 95% CI 8.2%–10.4%). According to WHO's classification of public health significance (moderate 20%–39.9%),

Table 2 Prevalence of anemia among women of reproductive age in China

	Anemia (95% CI)	Severity of anemia (95% CI)			
		Mild	Moderate	Severe	Moderate and worse
Overall	15.8 (15.1–16.6)	9.2 (8.8–9.7)	6.1 (5.8–6.5)	0.44 (0.41–0.48)	6.6 (6.3–7.0)
Body mass index					
< 18.5	14.2 (13.4–15.0)	9.4 (8.8–9.9)	4.6 (4.3–4.9)	0.21 (0.18–0.24)	4.8 (4.5–5.2)
18.5–23.9	16.3 (15.5–17.1)	9.8 (9.3–10.3)	6.1 (5.8–6.5)	0.42 (0.39–0.46)	6.6 (6.2–7.0)
24.0–27.9	15.7 (15.0–16.3)	8.4 (8.0–8.8)	6.7 (6.4–7.0)	0.56 (0.52–0.61)	7.3 (6.9–7.7)
⩾ 28.0	13.7 (13.0–14.3) [b]	7.2 (6.8–7.5) [b]	6.0 (5.7–6.3) [b]	0.52 (0.47–0.57) [b]	6.5 (6.2–6.9) [b]
Hypertension					
No	15.9 (15.1–16.6)	9.4 (8.9–9.8)	6.1 (5.7–6.4)	0.44 (0.40–0.48)	6.5 (6.2–6.9)
Yes	15.2 (14.6–15.7) [a]	7.7 (7.4–8.0) [b]	7.0 (6.7–7.3) [b]	0.50 (0.47–0.54) [b]	7.5 (7.2–7.9) [b]
Diabetes					
No	15.9 (15.1–16.6)	9.3 (8.8–9.7)	6.1 (5.8–6.5)	0.44 (0.41–0.48)	6.6 (6.3–7.0)
Yes	11.6 (11.1–12.2) [b]	5.4 (5.1–5.8) [b]	5.3 (5.0–5.6) [b]	0.53 (0.45–0.61) [a]	5.9 (5.5–6.2) [b]
High total cholesterol					
No	17.0 (16.2–17.8)	9.8 (9.3–10.2)	6.7 (6.3–7.0)	0.53 (0.49–0.58)	7.2 (6.8–7.6)
Yes	11.5 (10.9–12.1) [b]	7.3 (6.9–7.7) [b]	4.1 (3.9–4.3) [b]	0.10 (0.09–0.12) [b]	4.2 (4.0–4.4) [b]
High triglyceride					
No	16.3 (15.6–17.1)	9.5 (9.1–10.0)	6.3 (6.0–6.6)	0.46 (0.43–0.50)	6.8 (6.4–7.1)
Yes	12.4 (11.7–13.0) [b]	7.1 (6.6–7.6) [b]	4.9 (4.7–5.2) [b]	0.31 (0.29–0.34) [b]	5.2 (5.0–5.5) [b]
Hyperuricemia					
No	16.4 (15.7–17.1)	9.5 (9.1–10.0)	6.4 (6.1–6.8)	0.47 (0.43–0.51)	6.9 (6.5–7.3)
Yes	9.3 (8.7–10.0) [b]	6.2 (5.7–6.7) [b]	3.0 (2.8–3.2) [b]	0.16 (0.14–0.18) [b]	3.1 (2.9–3.4) [b]
History of cesarean delivery					
No	15.7 (14.9–16.4)	9.2 (8.7–9.6)	6.1 (5.7–6.4)	0.44 (0.40–0.47)	6.5 (6.2–6.9)
Yes	18.3 (17.0–19.6) [b]	10.4 (9.7–11.2) [a]	7.3 (6.7–7.9) [a]	0.55 (0.49–0.62) [b]	7.9 (7.3–8.6) [b]
Impaired kidney function					
No	15.8 (15.1–16.5)	9.2 (8.8–9.7)	6.1 (5.8–6.5)	0.44 (0.41–0.48)	6.6 (6.2–6.9)
Yes	31.9 (24.3–39.4) [b]	20.7 (9.4–32.1) [a]	9.9 (4.7–15.1)	1.22 (0.47–1.97) [a]	11.1 (5.3–17.0)

Abbreviations: CI, confidence interval; GDP, gross domestic product. Moderate and worse includes participants with moderate and severe anemia. [a]$P < 0.05$; [b]$P < 0.0001$.

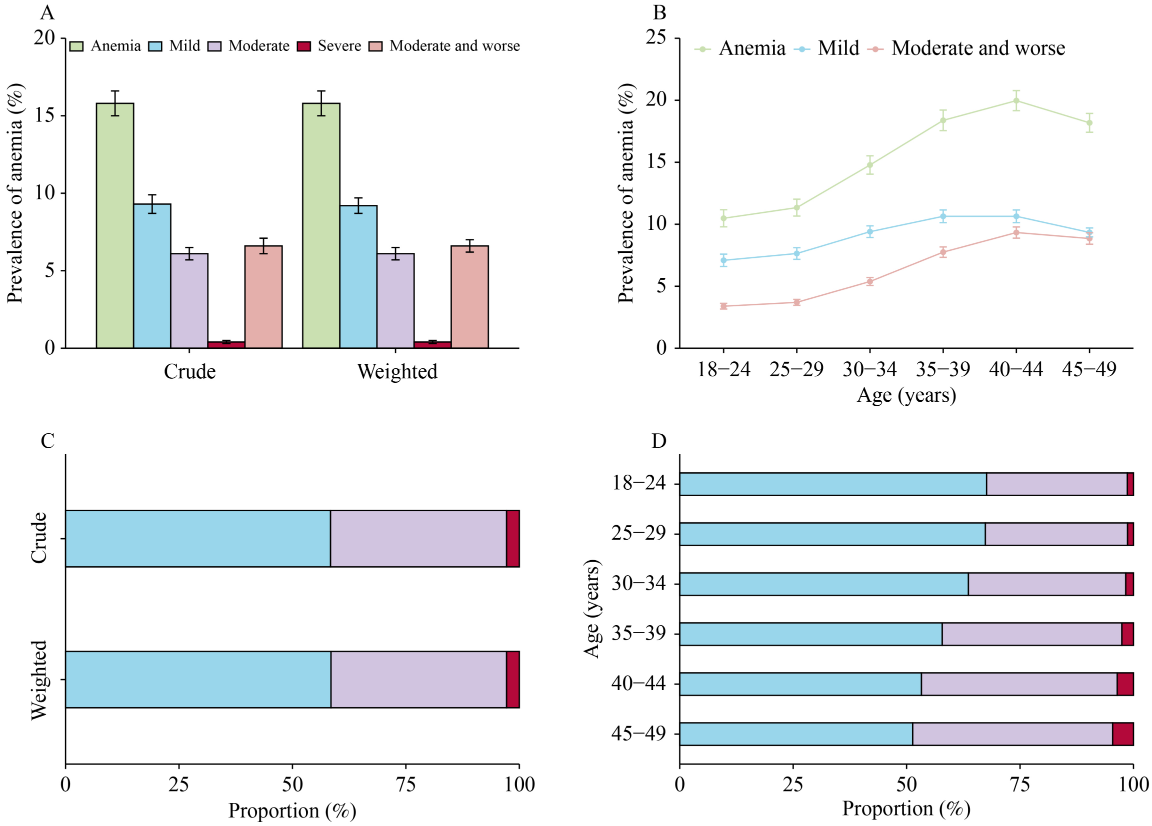

Fig. 1 Prevalence of anemia among women of reproductive age in China stratified by age and severity. (A) Crude and weighted prevalence of anemia, overall and by severity. (B) Age-specific prevalence of overall, mild anemia, and moderate and worse anemia. (C) Proportion of anemia of varying severity. (D) Proportion of anemia of varying severity stratified by age. Error bars represent the 95% CI. Moderate and worse includes moderate and severe anemia.

the prevalence reached moderate significance in two provinces, whereas the number of provinces reached 10 when focused on women aged 35–49. After adjustment for covariates, a higher likelihood of anemia was observed in south China (OR 1.67, 95% CI 1.40–2.00), central China (1.49, 1.22–1.82), and northwest China (1.47, 1.17–1.84) than that in southwest China (Table S7). Moderate and worse anemia ranged from 3.9% to 13.4%, with a higher prevalence in northwest China (OR 1.69, 95% CI 1.35–2.11) and north China (1.62, 1.34–1.97) than that in southwest China. The prevalence of anemia ranged from 7.3% to 25.2% among women aged 18–34, whereas the prevalence ranged from 11.2% to 25.1% among women aged 35–49. Similar patterns were observed for anemia of varying severity among women of different ages (Tables S8 and S9). The ecological analyses showed that the prevalence of moderate and worse anemia was negatively associated with per capita consumption of vegetables and fruits but positively associated with cereal and sugar.

Associations between metabolic risk factors and anemia

Women with overweight and obesity and hypertension had a lower prevalence of overall anemia than normal women, whereas moderate and worse anemia was higher among overweight and obese and hypertensive women (Table 2). Across all anemia of varying severity, the prevalence of anemia was higher among women with IKF than that in the corresponding group; however, this pattern was reversed in terms of diabetes, high TC, high TG, and hyperuricemia. Tables 3 and S10 show the results of multivariate logistic regressions. Older age (OR 1.20, 95% CI 1.19–1.21), IKF (2.38, 1.76–3.22), and history of cesarean delivery (1.16, 1.09–1.23) were positively associated with overall anemia; however, the associations were reversed for overweight and obesity, hypertension, diabetes, high TC, high TG, and hyperuricemia. With regard to moderate and worse anemia, overweight and obesity and diabetes were positively associated with moderate and/or severe anemia. In particular, diabetes in treatment or IKF significantly increased the likelihood of severe anemia (Table S11).

The nonlinear analysis indicated disparities in the associations between BMI and anemia of varying severity (Fig. 3). When BMI was over 23 kg/m^2, the association between BMI and mild anemia was negative and increasingly strengthened. By contrast, the association for

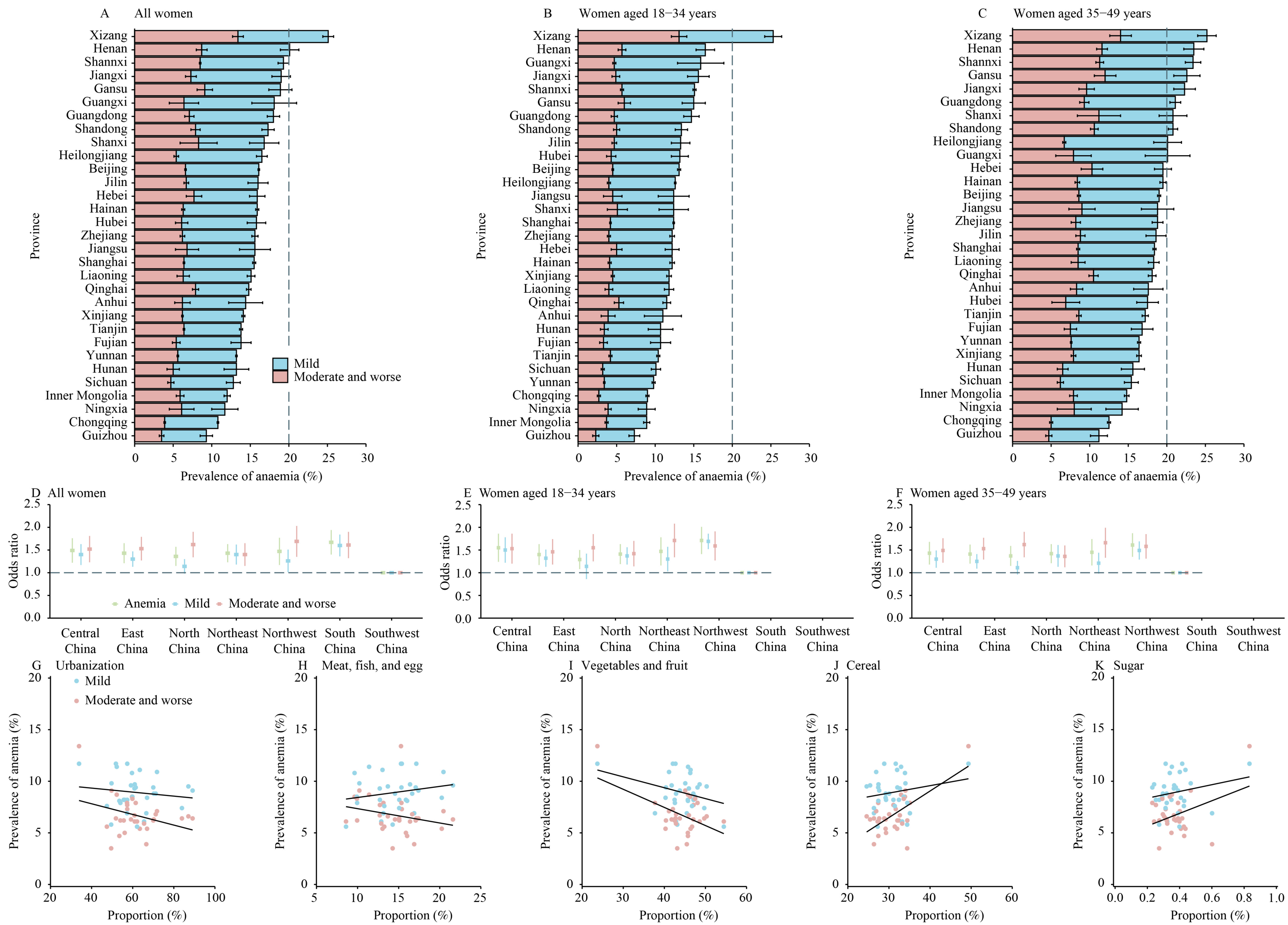

Fig. 2 Geographic variations in the standardized prevalence of anemia of varying severity among women of reproductive age and correlation with urbanization and per capita annual consumption of main food. The top panels show the provincial prevalence of anemia of varying severity among (A) all women, (B) women aged 18–34 years, and (C) women aged 35–49 years. Error bars represent the 95% CI of anemia. Vertical dashed lines indicate the threshold (20%) of moderate public health significance recommended by WHO. The middle panels present the variations by seven geographic regions among (D) all women, (E) women aged 18–34 years, and (F) women aged 35–49 years. The bottom panels show the ecological correlation between anemia and (G) urbanization and the proportion of per capita annual consumption of main food, including (H) meat, fish, and egg, (I) vegetables and fruits, (J) cereal, and (K) sugar. Linear regression was used to estimate the relationship coefficients.

Table 3 Multivariable-adjusted odds ratio for anemia among women of reproductive age in China

Independent variables	Anemia		Moderate and worse anemia	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (per 5 years)	1.20 (1.19–1.21)	< 0.0001	1.31 (1.29–1.31)	< 0.0001
Body mass index				
< 18.5	0.99 (0.97–1.00)	0.07	0.92 (0.90–0.94)	< 0.0001
18.5–23.9	Reference		Reference	
24.0–27.9	0.93 (0.92–0.94)	< 0.0001	1.02 (1.00–1.04)	0.04
⩾ 28.0	0.91 (0.88–0.94)	< 0.0001	1.04 (1.01–1.07)	0.02
Hypertension				
No	Reference		Reference	
Yes	0.89 (0.87–0.91)	< 0.0001	0.96 (0.94–0.98)	0.0001
Diabetes				
No	Reference		Reference	
Yes	0.75 (0.72–0.79)	< 0.0001	0.82 (0.79–0.85)	< 0.0001
High total cholesterol				
No	Reference		Reference	
Yes	0.59 (0.57–0.61)	< 0.0001	0.47 (0.46–0.49)	< 0.0001
High triglyceride				
No	Reference		Reference	
Yes	0.78 (0.75–0.82)	< 0.0001	0.75 (0.73–0.77)	< 0.0001
Hyperuricemia				
No	Reference		Reference	
Yes	0.62 (0.59–0.64)	< 0.0001	0.51 (0.48–0.53)	< 0.0001
Impaired kidney function				
No	Reference		Reference	
Yes	2.38 (1.76–3.22)	< 0.0001	2.00 (1.02–3.95)	0.045
History of cesarean delivery				
No	Reference		Reference	
Yes	1.16 (1.09–1.23)	< 0.0001	1.17 (1.10–1.25)	< 0.0001

OR, odd ratio; CI, confidence interval; GDP, gross domestic product. Moderate and worse includes moderate and severe anemia.

moderate anemia was insignificant and then changed to positivity when BMI was over 28 kg/m^2. Differently, the negative association between severe anemia and BMI rapidly attenuated before 23 kg/m^2 and then sharply changed to positivity and continuously strengthened.

Sensitivity analyses showed no significant interaction terms in the models (data not shown) and similar results to our main analyses when using data without missing values (Table S12).

Discussion

To the best of our knowledge, this study was the first to estimate the prevalence of anemia of varying severity and geographic variations among women of reproductive age in China with a considerably large sample size and on a regional scale. The anemia prevalence was estimated at 15.8% among reproductive women in 2019, corresponding to 45.7 million anemic cases. Of them, 19.0 million were moderate and worse anemia. The anemia prevalence was more than 20% among women aged 35–49 years in 10 provinces, indicating a public health concern of anemia in China. Furthermore, we found a significant association between anemia and metabolic risk factors. In particular, moderate and worse anemia was positively associated with BMI. These findings not only identified a high-risk group of anemia for targeted intervention but also suggested the identification and management of metabolic disorders in the anemia reduction strategy.

Our result in anemia prevalence was similar to the estimation by GBD 2021, which was lower than those in Japan (19.0%), Russia (21.0%), Indonesia (31.0%), and India (53.0%) but higher than those in the Republic of Korea (14.0%), America (12.0%), the UK (11.0%),

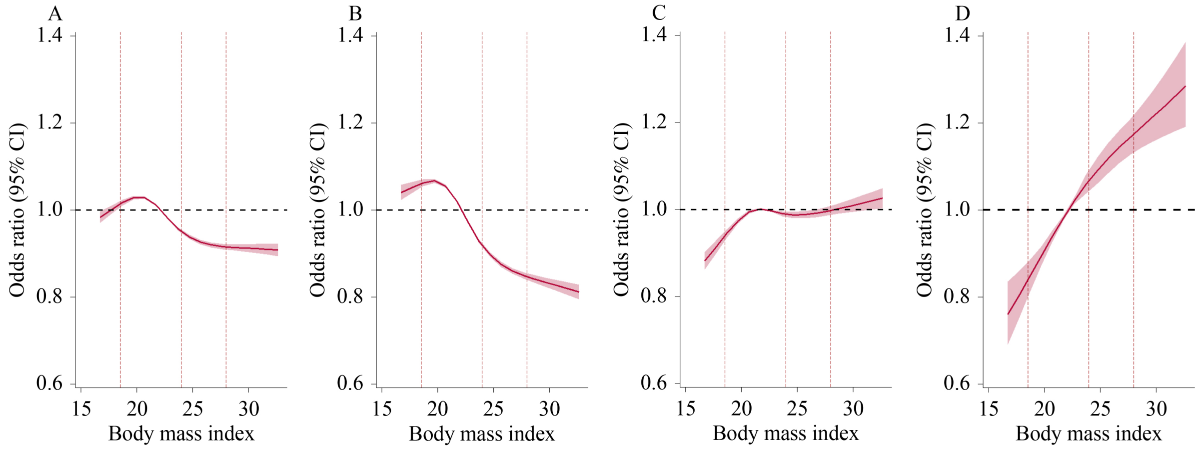

Fig. 3 Difference in the nonlinear associations of (A) anemia, (B) mild anemia, (C) moderate anemia, and (D) severe anemia with BMI. Lines represent odd ratios estimated from a logistic regression between anemia and BMI, adjusted for hypertension, diabetes, high total cholesterol, high triglyceride, hyperuricemia, impaired kidney function, city-level per capita GDP, province-level unemployment, and province-level education. BMI was fitted as a four-knot restricted cubic spline as the 5th, 35th, 65th, and 95th percentiles to allow for nonlinearity. *P* values for overall association and nonlinearity were less than 0.0001 for all outcomes. Vertical lines represent BMI category thresholds of 18.5 kg/m^2 (underweight to healthy), 24 kg/m^2 (healthy weight to overweight), and 28 kg/m^2 (overweight to obese).

Canada (10.0%), and the European Union (14.0%) [4]. Moreover, the prevalence of overall and severe anemia was similar to or even higher than that from the Chinese nutrition surveillance (15.4%) [7] and national preconception health examination project (0.24%) [8] in 2012, indicating potentially increasing risk of anemia among this group. A similar pattern was observed in low- and middle-income countries [17]. Although our estimation was lower than that among pregnant women [18,19], the studied group is more likely to become pregnant and show advanced severity of anemia and then adverse outcomes during the perinatal period [20]. In China, the control of anemia mainly focuses on children, pregnant women, and older women but does not include reproductive women [21]. According to our results, the comprehensive strategy should pay considerable attention to reproductive women and undertake action to reduce the burden of anemia.

Consistent with previous studies [8,18], our study showed that older age was positively associated with anemia, especially for moderate and severe anemia. This association is mainly due to micronutrient deficiencies, infections, inflammation, and chronic diseases [1], which would rise with age. Stem cell aging, testosterone deficiency, and myelodysplastic disorders also decrease erythrocyte production or shorten lifespan [22]. This finding has great implications for the management of anemia for reproductive women in two ways. First, despite the low prevalence of anemia, women younger than 25 still require special attention because they have a higher risk of anemia during pregnancy than their counterparts and are more likely to become pregnant [23]. Second, in the context of the three-child policy in China, the childbearing age would be delayed, and more women older than 35 would become pregnant. Hence, screening, early identification, and management of moderate and worse anemia are critical for those preparing for pregnancy at an older age. The association between mild anemia and poor maternal and fetal outcomes remains controversial [23,24], and further studies on the optimal concentration of Hb for reproductive women are needed.

Our results found large geographic variations in the prevalence of anemia of varying severity, which could be partly explained by the differences in dietary structure, particularly the consumption of vegetables and fruits, cereal, and sugar. The variation was mainly caused by the substantially higher prevalence of anemia in Xizang than that in other provinces. Except for high altitude [25], the case may be linked to folic acid or vitamin B12 deficiency resulting from dietary imbalance, i.e., a lower proportion of vegetables and fruits but a high proportion of cereal and sugar. Consistent with the previous study [26], our results implied that the anemia reduction strategy should attach importance to a balanced dietary structure and nutrient supplements rather than iron intervention only. The high burden of anemia in south China was associated with the high prevalence of thalassemia in Guangdong and Guangxi provinces [27]. By contrast, the anemia prevalence in southwest China, especially in Guizhou Province, was lower than what was previously believed. This finding could be attributed to the implementation of a nutrition and screening program for the central and local population [28]. In the future, extensive local data on anemia subtypes, such as iron-deficiency anemia, megaloblastic anemia, and sideroblastic anemia, could help identify the underlying cause of variations and targeted subgroups.

This study identified a significant correlation between overweight or obesity and a high likelihood of severe anemia, as well as an insignificant correlation with moderate anemia. This finding could be explained by various biological mechanisms, such as persistent inflammation resulting in iron insufficiency and defects in Hb formation, nutritional imbalance, increased iron requirements, limited myoglobin storage capacity due to low physical effort, and genetic susceptibility [5]. The negative association between BMI and mild anemia may be attributed to high energy protein intake, which was also observed in previous studies in China [29,30].

Hypertension and hyperlipidemia were negatively associated with anemia, in line with previous studies [31,32]. The low alcohol consumption among Chinese women means that hyperuricemia generally represents enhanced nutrient intake. Uric acid could protect red blood cells by correcting metabolic disorders, supporting the negative association between anemia and hyperuricemia [33]. Previous studies found a high risk of anemia in poorly controlled diabetes, diabetes with renal insufficiency, and chronic kidney function [34–36]. Our results proved a high anemia prevalence among individuals with IKF. Although diabetes was negatively associated with overall anemia, further classification indicated that diabetes in treatment and diabetic nephropathy were associated with increased odds of moderate and worse anemia. These results revealed complicated associations between anemia and metabolic risk factors among reproductive women. The management of metabolic risk factors could not only reduce the risk of anemia but also increase the likelihood of exacerbation of existing anemia due to inappropriate intervention measures among those who had anemia and metabolic disorders. In consideration of the increasing prevalence of metabolic risk factors, our results suggest timely identification and management of metabolic risk factors in the comprehensive strategy for anemia reduction.

This work is an updated nationwide study on anemia in the mainland of China since 2012, which included more than 4 million women of reproductive age in 231 cities from all 31 provinces. Thus, our results are robust in the stratified estimation of anemia prevalence among the subgroup population. However, some limitations should be considered. First, the overall anemia prevalence represents the condition in urban areas in consideration of the characteristics of participants. Second, the Hb concentration was not adjusted for smoking status because of the unavailability of data about smoking dose. Nonetheless, the case would not affect the estimation because of the extremely low smoking prevalence among Chinese women. We could not identify the subtype of anemia owing to a lack of clinical records, and further studies are needed for individual intervention measures. Furthermore, the prevalence of metabolic disorders in this study might have been underestimated, e.g., one-time FPG for diabetes diagnosis rather than oral glucose tolerance test and glycosylated Hb test.

Conclusions

Our study found a relatively high prevalence of anemia of varying severity among women of reproductive age in China. Comprehensive and targeted intervention strategies for anemia reduction should consider the geographic variations and characteristics of metabolic factors in the population.

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Compliance with ethics guidelines

Conflict of interest Heling Bao, Yuanyuan Huang, Yi Sun, Yunli Chen, Yan Luo, Liping Yan, Sailimai Man, Canqing Yu, Jun Lv, Meili Ge, Linhong Wang, Xiaoxi Liu, Hui Liu, Bo Wang, and Liming Li declare that they have no competing interests.

The study was approved by the Peking University Institution Review Board (IRB-0000152-19077), and individual informed consent was waived because anonymous data were used.

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