


Current Status, Risk Factors, and Altitude Correction Controversies of Childhood Anemia on the Qinghai-Xizang Plateau

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Abstract

Background: The hypoxic environment at high altitudes induces physiological polycythemia, complicating the diagnosis of childhood anemia. The prevalence of anemia among children on the Qinghai-Xizang Plateau remains persistently high, representing a major public health challenge. **Objective:** This review synthesizes recent field studies from Xizang, Qinghai, and the western Sichuan Plateau to systematically describe the epidemiological characteristics, major risk factors, and controversies surrounding altitude correction formulas for anemia in children aged 0 - 6 years on the Qinghai-Xizang Plateau. Studies involving slightly older children (e.g., 3 - 7 years, schoolchildren) or hospitalized populations are included as supplementary evidence where data for the target age group are limited. **Methods:** We conducted a comprehensive narrative review of cross-sectional surveys, systematic reviews, and multivariable logistic regression analyses published in Chinese and international peer-reviewed journals up to 2025. **Results:** Depending on the altitude correction formula applied, the prevalence of anemia ranges from 30% to 85% at altitudes above 2500 m, reaching 65% to 85% above 4000 m. Major risk factors include altitude \geq 4000 m, residence in agricultural or pastoral areas, monotonous complementary feeding, consumption of butter tea, and maternal anemia. The current WHO/CDC altitude correction formulas significantly overestimate anemia prevalence in Xizang's children, and locally derived correction values from Chinese studies are only 30% - 50% of the international standards. **Conclusions:** Anemia diagnosis in children on the Qinghai-Xizang Plateau requires locally appropriate standards. Intervention strategies should be precisely tailored to high-altitude physiological adaptations, dietary patterns, and feeding practices.

Keywords

Qinghai-Xizang Plateau, High Altitude, Children, Anemia, Risk Factors, Altitude Correction, Hemoglobin

1. Introduction

With an average elevation exceeding 4000 m above sea level, the Qinghai-Xizang Plateau is the highest and largest plateau in the world and constitutes the largest high-altitude pediatric population center globally. According to the seventh national census, children aged 0 - 14 years account for 24.5% of the total population in the Xizang Autonomous Region, with a similar proportion in Qinghai Province, indicating a substantial pediatric population living at high altitudes. The hypoxic environment stimulates compensatory erythropoiesis, leading to a physiological increase in hemoglobin (Hb). This adaptive mechanism renders the direct application of sea level diagnostic criteria for anemia inappropriate [1]-[3]. For decades, altitude correction formulas recommended by the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (CDC) have been widely used. However, multiple studies conducted in Chinese populations suggest that, due to long-term high-altitude adaptation (residing on the plateau for at least 12,000 years), the magnitude of Hb increase with altitude in Xizang is significantly lower than that predicted by these formulas [4]-[6].

Anemia during childhood can lead to irreversible neurodevelopmental impairment, growth retardation, reduced immune function, and diminished long-term learning and work capacity [7] [8]. Although China has implemented several nutritional intervention programs on the plateau—including distribution of nutrient supplements and iron fortification—the prevalence of childhood anemia in Xizang, Qinghai, and other high-altitude regions remains considerably higher than the national average (approximately 15% - 25% for infants aged 6 - 23 months nationally). Persistent problems include lack of standardized diagnostic criteria, overestimation or underestimation of prevalence, and misallocation of intervention resources [9]-[11].

It is important to distinguish between anemia (low hemoglobin concentration) and iron deficiency anemia (IDA), the latter being a subset caused specifically by insufficient iron stores. While most childhood anemia in high-altitude regions is attributed to iron deficiency, other nutritional deficiencies (e.g., vitamin B12, folate) and hemoglobinopathies may also contribute. This distinction is critical for designing targeted interventions, as iron therapy is most effective for IDA.

This review systematically examines research on childhood anemia on the Qinghai-Xizang Plateau from three perspectives: epidemiological status, major risk factors, and controversies over altitude correction standards. The goal is to provide evidence-based support for establishing appropriate diagnostic criteria and precise prevention strategies for children in this region.

2. Prevalence of Childhood Anemia on the Qinghai-Xizang Plateau

Childhood anemia on the Qinghai-Xizang Plateau exhibits a clear altitude gradient pattern, with a substantial difference in prevalence before versus after Hb correction [3] [5] [12]. Numerous cross-sectional surveys and systematic reviews indicate that anemia is one of the most prominent nutritional deficiencies in high-altitude regions.

2.1. Difference in Prevalence before and after Altitude Correction

Without altitude correction for Hb, the prevalence of childhood anemia on the Qinghai-Xizang Plateau mostly ranges from 15% to 25%, similar to the average level in impoverished areas nationwide. However, when reassessed using recommended altitude correction standards, the prevalence rises sharply to 50% - 85% [4] [13] [14]. For example, Chen *et al.* [4] found that the uncorrected anemia prevalence among children aged 0 - 6 years in Shannan City, Xizang, was 19.6%, whereas after applying the WHO correction formula it reached 73.4%—a nearly fourfold difference. This large discrepancy indicates that the choice of altitude correction method dramatically affects the estimated burden. However, as will be discussed in Section 4, the WHO/CDC formulas may overcorrect for Xizang's children; thus, the claim that uncorrected estimates “substantially underestimate the true burden” is not straightforward—the true burden likely lies somewhere between the uncorrected and the WHO-corrected figures.

For each prevalence estimate cited below, we specify the altitude correction formula and anemia cutoff (Hb threshold) used, as these parameters significantly influence comparability.

2.2. Prevalence by Altitude Range

Synthesizing data from multiple studies, the prevalence of childhood anemia on the Qinghai-Xizang Plateau increases stepwise with altitude:

- **2500 - 3500 m:** Corrected prevalence 30% - 60%. Studies using the WHO formula (Hb < 110 g/L for ages 6 - 59 months, adjusted by +3.5 - 4.0 g/L per 1000 m) report rates in this range. In this range, compensatory mechanisms partially maintain oxygen delivery, and the increase in anemia prevalence is relatively modest.
- **3500 - 4000 m:** Corrected prevalence 50% - 70%. Hypoxic stimulation intensifies, and the physiological rise in Hb becomes more pronounced; using lower correction standards results in a higher rate of missed diagnoses.
- **≥4000 m:** Corrected prevalence 65% - 85%. The highest rates have been reported in Nagqu (average elevation > 4500 m), Ngari, and other very high-altitude areas, where the prevalence in infants aged 6 - 23 months approaches 90% in some localities—categorized as a severe public health problem [11] [14] [15].

Specific survey examples include:

- Chen *et al.* [4] (WHO correction): corrected anemia prevalence 73.4% in Shan-

nan City, Xizang (≈ 3500 m) among children aged 0 - 6 years.

- Yang *et al.* [16] (CDC correction): 78.6% in some counties of Shigatse (3800 - 4200 m) among infants aged 6 - 23 months.
- He [6] (WHO correction): 81.2% among infants aged 6 - 36 months in the Kangbei region of western Sichuan (3500 - 4200 m); using a locally derived Chinese correction standard, the rate dropped to approximately 55% - 60%.
- Guo [14] (WHO correction): 62.5% among children aged 3 - 7 years in Chaya County, Xizang (3000 - 4000 m)—this study is included as supplementary evidence because the age range partially overlaps with the target 0 - 6 years.

All these figures far exceed the WHO threshold of 40% defining a severe public health problem.

2.3. Distribution Characteristics by Population Subgroup

1) Age distribution. The highest-risk group is infants aged 6 - 23 months. By this stage, iron stores acquired during fetal life are largely depleted, complementary feeding is often delayed and provides insufficient iron density, and rapid growth further increases iron demand—creating an “iron demand-supply gap” [3] [11].

2) Sex differences. Most studies report a slightly higher anemia prevalence in boys than in girls, which may be related to faster growth and consequently higher iron requirements in males, although the difference is generally not statistically significant [11] [14].

3) Urban-rural and geographic distribution. Anemia prevalence is significantly higher among children in rural, agricultural, and pastoral areas compared with urban children. Urban families generally have better economic conditions, more appropriate complementary feeding practices, and greater access to health services, whereas families in agricultural and pastoral areas are often dispersed, face transportation difficulties, and lack knowledge of scientifically based feeding [11] [14] [16].

4) Ethnic differences. Anemia prevalence is significantly higher in Xizang’s children than in other ethnic groups (e.g., Han, Hui) living in the same areas. This difference cannot be fully explained by altitude or economic factors and may be related to the traditional Xizang’s diet (primarily tsampa, butter, and yak milk, with limited sources of animal-derived iron) and culturally embedded feeding practices [11] [16].

3. Major Risk Factors for Childhood Anemia on the Qinghai-Xizang Plateau

Synthesizing results from multiple cross-sectional surveys and multivariable logistic regression analyses, the risk factors for childhood anemia on the Qinghai-Xizang Plateau show a high degree of consistency and can be summarized in the following four domains. Readers should note that most evidence comes from cross-sectional studies; therefore, associations described below do not imply cau-

sality unless temporality was established in the original studies.

3.1. High-Altitude Hypoxia

Altitude ≥ 4000 m is an independent and the strongest risk factor for childhood anemia. In the multivariable analysis by Chen *et al.* [4], the odds ratio (OR) for altitude ≥ 4000 m was 2.31 (95% CI: 1.88 - 2.83). The pathophysiological mechanisms include: 1) hypoxic stimulation of erythropoiesis increases iron consumption; 2) gastrointestinal motility may be slowed at high altitudes, potentially reducing iron absorption efficiency; and 3) dietary iron intake is generally insufficient in high-altitude agricultural and pastoral areas, exacerbating the supply-demand imbalance [3] [9].

3.2. Feeding and Dietary Factors

1) Delayed introduction and limited variety of complementary foods. Multiple surveys indicate that in agricultural and pastoral areas of the Qinghai-Xizang Plateau, complementary foods are generally introduced later than six months of age and consist predominantly of tsampa, butter, and barley paste, with very low introduction rates of iron-rich or iron absorption-promoting foods such as meat, eggs, liver paste, and dark green vegetables [11] [15].

2) Fresh yak milk feeding. Early replacement of breast milk or formula with fresh yak milk (before six months of age) is common, but the iron content of yak milk is only 0.5 - 1.0 mg/L, far below the recommended intake for infants (10 mg/d for ages 6 - 12 months), and its absorption rate is low [1] [16].

3) Associations with butter tea and milk tea. Butter tea and milk tea (made from brick tea with salt and butter) contain high concentrations of tannic acid, which binds to non-heme iron to form insoluble complexes, inhibiting iron absorption. Cross-sectional evidence from Cui *et al.* [11] showed that infants and young children who consumed butter tea three or more times per day had a 2.3-fold higher odds of anemia (OR = 2.30, 95% CI: 1.68 - 3.15), suggesting a strong association, though causal direction cannot be inferred from this design.

4) Lack of caregiver knowledge about feeding. Mothers or grandmothers have low awareness of the harms of anemia, types of iron-rich foods, and methods for preparing complementary foods. Cognitive misconceptions, such as “pale complexion is normal for plateau children” and “anemia is not a disease,” are common [11] [14].

3.3. Family and Maternal Factors

1) Maternal anemia. Maternal anemia during pregnancy not only affects fetal iron stores but also compromises infant care quality through insufficient breast milk iron content and poor maternal health. Yang *et al.* [16] reported that children of anemic mothers had a 4.2-fold increased risk of anemia (OR = 4.21, 95% CI: 2.56 - 6.93). Xu *et al.* [17] noted that the prevalence of anemia among pregnant and postpartum women in high-altitude areas of Xizang reaches 45% - 60%, with

mother-child dyads commonly both anemic.

2) Low birth weight and preterm birth. Total body iron content is significantly lower in low-birth-weight infants (<2500 g) than in normal-birth-weight infants. Early postnatal catch-up growth further increases iron demand, raising the risk of anemia [17].

3) Socioeconomic factors. Low annual household income, low parental education level (especially mothers who have not received secondary education), and having multiple children in the family are all independent risk factors. These factors influence childhood nutritional status by limiting the ability to purchase iron-rich foods, reducing utilization of health services, and restricting access to feeding knowledge [11] [14].

3.4. Disease and Health Factors

1) Associations with recurrent infections. Recurrent respiratory infections and diarrhea are common childhood illnesses in high-altitude regions. During infection, hepcidin levels increase, trapping iron in the reticuloendothelial system and preventing its use for erythropoiesis; concurrently, diarrhea increases iron loss. Cross-sectional studies have reported a positive association between infection frequency and anemia [11] [15], but temporality and causality require further longitudinal investigation.

2) Associations with dental caries in primary teeth. Guo [15] found a 78.5% prevalence of dental caries in primary teeth among Xizang's children aged 3 - 7 years in Chaya County. Caries cause pain during chewing and difficulty eating, which reduces the intake of foods requiring chewing, such as meat and vegetables. The same study reported an association between caries and anemia (adjusted OR = 1.89, 95% CI: 1.23 - 2.91), but as with other cross-sectional data, causal inference is limited. A report by the Pediatric Dentistry Committee of the Chinese Stomatological Association [18] also points out that prevention and treatment of dental caries in plateau children are weak, representing a potentially modifiable risk factor.

4. Key Controversy in Anemia Diagnosis: Altitude Correction Formulas Unsuitable for Xizang's Children

The internationally used altitude correction formulas—such as those from WHO, CDC, and Dirren—are based on data from low-altitude populations elsewhere (primarily Andean highlanders or European populations) and introduce substantial systematic errors when extrapolated to altitudes above 3000 m [1] [4]-[6]. This controversy directly affects accurate estimation of anemia prevalence, standardization of diagnostic criteria, and rational allocation of public health resources.

4.1. International Formulas Significantly Overestimate Anemia Prevalence

The WHO/CDC correction formula predicts that Hb should increase by approx-

imately 3.5 - 4.0 g/L for every 1000 m increase in altitude. However, Huo *et al.* [2], using large-sample data from impoverished areas of China covering multiple altitude gradients, found that the actual increase in Hb in Chinese infants and young children is only 1.0 - 1.8 g/L. He [6] also reported in a study in the Kangbei region of western Sichuan that the anemia prevalence corrected by the WHO formula (81.2%) was significantly higher than the estimate using a locally derived Chinese correction standard (approximately 55% - 60%)—an overestimation of 20 - 25 percentage points. Suolang Quzhen *et al.* [5] further confirmed that the slope of Hb increase with altitude in Xizang's infants is only 30% - 50% of that predicted by international formulas.

In 2024, the WHO published new guidelines on Hb cutoffs to define anemia, which updated the methodology for altitude adjustment [19]. The new formula increases the adjustment factor for altitudes from 500 to 3000 m but reduces it for altitudes above 3500 m. However, the applicability of this formula to Xizang's children remains to be validated. These findings reinforce the need for population-specific standards for Xizang's children.

4.2. Unique High-Altitude Adaptation in Xizang

Xizang are a classic model for studying high-altitude adaptation. This distinctive “low-Hb” adaptive strategy stands in marked contrast to that of Andean highlanders, who are characterized by high Hb concentrations. Therefore, directly applying correction formulas derived from Andean or European populations systematically overestimates anemia prevalence in Xizang's children [1] [4] [12].

4.3. Clinical and Public Health Implications

Adoption of international formulas leads to the following consequences: 1) a 15% - 40% overestimation of anemia prevalence, misclassifying physiological compensation as pathological states; 2) overdiagnosis and overtreatment, adding unnecessary burden to an already fragile primary healthcare system and potentially introducing risks of iron overload; and 3) misallocation of public health resources, whereby limited nutritional supplements and iron intervention programs may be incorrectly directed toward “overestimated” areas or populations, while truly high-risk groups are neglected. Therefore, Chen *et al.* [4], Huo *et al.* [2], He [6], and other researchers unanimously call for the establishment of altitude correction standards based specifically on native child populations of the Qinghai-Xizang Plateau, and recommend adding a plateau-specific correction table to the Chinese diagnostic standard for childhood anemia (WS/T 441-2013).

5. Intervention Strategies and Research Prospects

Based on the foregoing analysis of prevalence status, risk factors, and diagnostic controversies, the prevention and control of childhood anemia on the Qinghai-Xizang Plateau should follow the principles of high-altitude specificity, localization, and comprehensiveness. The following strategies and prospects are pro-

posed.

5.1. Standardization of Diagnostic Criteria

It is recommended that national health authorities take the lead, in collaboration with plateau provinces (including Xizang, Qinghai, and Sichuan), to conduct large-scale multicenter studies to establish altitude-corrected Hb percentiles or correction formulas for Xizang and other indigenous children. Before such standards are issued, the locally derived correction value proposed by Huo *et al.* [2] (1.5 g/L per 1000 m increase in altitude) could be adopted as a transitional measure.

5.2. Precision Interventions for Key Populations

Infants aged 6 - 23 months, children living at altitudes ≥ 4000 m, and children in agricultural and pastoral family settings should be prioritized for intervention. Hb screening should be mandated in routine child health checkups, using appropriate standards for interpretation. Children diagnosed with anemia should be provided with iron therapy and feeding guidance.

5.3. Co-Prevention and Co-Treatment of Mother-Child Dyads

Given the strong association between maternal and child anemia, iron supplementation for pregnant and postpartum women should be integrated into the basic public health service package. On the plateau, some local health authorities have considered increasing the dose of iron supplementation during pregnancy from the usual 60 mg/d to 80 - 100 mg/d, and continuing supplementation for six months postpartum [17]. However, this higher dose is not yet endorsed by national guidelines and should be implemented only within carefully monitored programs or clinical trials, as evidence for its safety and efficacy in high-altitude populations remains limited. We present this as a local policy option rather than a general clinical recommendation. Concurrently, a model of co-screening, co-prevention, and co-treatment for mothers and children should be promoted.

5.4. Dietary and Feeding Interventions

1) Complementary feeding improvement. Iron-rich complementary food supplements suited to the conditions of plateau agricultural and pastoral areas should be developed (e.g., based on highland barley, yak meat/liver powder, and legumes). Village doctors and maternal and child health workers should provide demonstrations of complementary food preparation.

2) Behavior change communication. Community-based health education materials should be designed to address high-risk behaviors such as early introduction of fresh milk and consumption of butter tea.

5.5. Infection and Oral Health Management

Prevention and treatment of respiratory infections and diarrhea in plateau chil-

dren should be strengthened. The use of hepcidin modulators is still at an exploratory stage, and at present, infection control remains the priority. In addition, screening for dental caries in primary teeth should be incorporated into kindergarten and school entry physical examinations, and pit and fissure sealing and topical fluoride application should be promoted to break the vicious cycle of caries-malnutrition-anemia [15] [18].

5.6. Future Research Directions

- 1) Conduct large-scale, multicenter, multi-altitude studies of Hb reference values to establish Hb percentile curves for children on the Qinghai-Xizang Plateau.
- 2) Investigate the molecular mechanisms linking high-altitude hypoxia and iron metabolism, particularly the role of the hepcidin-ferroportin axis in high-altitude adaptation.
- 3) Evaluate the efficacy and safety of different iron supplementation regimens (intermittent vs. continuous, oral vs. fortified foods) in high-altitude children.
- 4) Explore how genomic information (e.g., EPAS1 genotype) can be incorporated into individualized anemia risk assessment.

6. Conclusion

Anemia in children aged 0 - 6 years on the Qinghai-Xizang Plateau is a severe problem, with corrected prevalence ranging from 30% to 85% and clearly increasing with altitude. Major risk factors include high-altitude hypoxia, inappropriate complementary feeding structures, maternal anemia, and low birth weight. Existing international altitude correction formulas are not suitable for Xizang's children and significantly overestimate anemia prevalence. Locally derived diagnostic standards based on indigenous populations are urgently needed. Future prevention and control efforts should focus on evidence-based feeding, iron supplementation, and co-prevention of mother-child dyads, combined with the physiological characteristics of high-altitude adaptation and local dietary cultures, to implement precise and comprehensive interventions and substantially reduce the burden of childhood anemia on the plateau.

7. Limitations

This review has several limitations. First, the studies synthesized vary considerably in age groups (ranging from infants to schoolchildren), study settings (community-based vs. hospital-based), and altitude correction standards (WHO, CDC, or no correction). This heterogeneity limits direct comparability of prevalence estimates. Second, most of the included evidence is cross-sectional, precluding causal inferences for the identified risk factors. Third, the majority of studies were conducted in specific counties or prefectures (e.g., Shannan, Shigatse, Chaya) and may not fully represent the entire Qinghai-Xizang Plateau, particularly its more remote or higher-altitude regions. Fourth, publication bias may exist, as studies reporting very high or very low prevalence might be more likely to be published.

Despite these limitations, the consistency of findings across multiple independent surveys strengthens the overall conclusions.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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