

Revised WHO Guidelines on Hemoglobin Cutoffs to Define Anemia in Individuals and Populations

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ABSTRACT

In 2024, the World Health Organization (WHO) has proposed revised hemoglobin cutoffs for diagnosing anemia in children aged 6–23 months, pregnant women in the second trimester and those residing in elevated areas with the aim of increasing the sensitivity and ensuring uniformity in diagnosis. There are no major changes in other domains.

Keywords: Anemia, Altitude, Deficiency, Folic acid, Global health, Iron

Anemia continues to be a global health concern, affecting around 40% of the children aged 6-59 months, 30% of the women aged 15-49 years and 37% of the pregnant women worldwide, as per the World Health Organization (WHO) in 2019 [1]. There are multiple global health programs targeting anemia like the Global Nutrition Target 2025, the 2030 Sustainable Development Goals (SDGs), Comprehensive Implementation Plan on Maternal Infant and Young Child Nutrition and Global Strategy for Women's, Children's and Adolescent's Health (2016-2030). It was felt that appropriate guidelines for detecting and defining anemia will help in the efficient implementation of these programs for lowering the prevalence of anemia. The recent "WHO Guideline on the Hemoglobin Cutoffs to Define Anemia in Individuals and Populations" is in coherence with WHO's Thirteenth General Programme of Work 2019-2023, endorsed by the World Health Assembly in May 2018, specifically enabling countries to provide high-quality, people-centred health services [2]. The purpose of this guideline is to have uniform standards for the development of nutrition and health policies and so that no one is left behind [2-7].

A Steering Committee, led by the Department of Nutrition and Food Safety, was established in 2019, with representatives from relevant WHO departments with an interest in the provision of scientific nutrition advice. The Steering Committee guided and provided overall supervision of this guideline development process. Two additional groups were formed: the Guideline Development Group (GDG) and a systematic review team.

History

The first hemoglobin (Hb) cutoffs for anemia were defined by the WHO in 1959 [8]. The current cutoffs, which are followed for men, women, young children, and pregnant women, were recommended by the WHO in 1968; these were based on data from five studies of populations from Europe and North America. The data from other countries was scanty at that point, also data from certain populations like infants, children, adolescents and elderly people was not available then. In 2001, the WHO guidelines were revised again and new lower Hb cutoffs for children aged 5-14 years based on NHANES II data were issued; adjustments were made for those residing at higher altitudes and for smokers [9].

Summary of Evidence

There is paucity of data on Hb cutoffs for defining anemia based on reference population of healthy individuals after consideration of genetic and environmental factors which influence Hb. The evidence in these guidelines was based on analysis of Hb data from healthy populations, general population databases and

systematic reviews. For estimating the anemia cutoffs and confidence intervals, parametric method was employed as the reference distribution appeared reasonably normal. Data was pooled using fixed and random effects model [10].

Clinical Versus Statistical Outcomes

It was attempted to define cutoffs based on clinical symptoms or functional impairment due to anemia. However, due to lack of data on relevant outcomes and precise cutoffs, statistical approach was used. An important consideration was whether to use the 5th or 2.5th percentile for Hb cutoffs. To improve sensitivity (as in previous guidelines), 5th percentile was considered as the cutoff, which would imply that 95% of healthy individuals would have higher Hb value and 5% of healthy individuals will be falsely labelled as anemic. The higher of the two percentiles was selected to increase the detection of individuals with underlying conditions such as malnutrition, genetic disorders, inflammation, and infection. The 5th centiles of Hb distributions were largely obtained from higher-income countries questioning their applicability for Indian children.

Key Recommendations

a. Hemoglobin cutoffs to define any anemia

Separate Hb cutoffs for defining anemia are recommended for children aged 6–23 months. Hb cutoffs for defining anemia in pregnant women in the second trimester have been separately added considering that physiological changes occur in the second trimester that lead to an expansion in plasma volume alongside a smaller increase in red cell mass resulting in hemodilution. The updated cutoffs to define anemia in individuals and populations and their comparison with existing guidelines is given in **Table I**. **Tables II and III** depict the recommended adjustments in Hb cutoffs to determine anemia in persons living in higher altitudes.

b. Anemia severity

There is only a change in the Hb cutoffs to define anemia (mild anemia) in children aged 6-23 months and in pregnant women in the second trimester. Rest of the Hb cutoffs to determine the severity of anemia remain unchanged due to insufficient evidence (**Table I**).

Research Gaps

- Research needed on Hb cutoffs below which symptoms appear, morbidity increases, development is impaired etc.
 - Optimal criteria should be laid to define a healthy population
 - Future studies to define 5th percentiles for healthy populations from all geographical areas and age groups
- c. Hemoglobin adjustment for external factors:* While the cutoffs need to be adjusted for altitude, no change is recommended for the presence of infection/inflammation or for race/ethnicity/ancestry for the lack of enough evidence.
- d. Hemoglobin as an indicator of public health*

Current classification of the public health significance of anemia in population indicates it to be mild, moderate or severe, if prevalence of anemia is 5.0-19.9, 20.0-39.9 and $\geq 40\%$, respectively [12]. Association between public health significance of anemia with clinical and/or demographic outcomes has been used for planning, initiating, implementing, and evaluating country-specific or regional plans to address anemia. The current

classification of the public health significance of anemia is based on expert opinion alone. WHO recommends no change in this definition, until new evidence becomes available.

Change in Hb should be used as a marker to assess the impact of interventions (e.g. iron supplementation and staple food fortification with iron and other vitamins and minerals) for both prevention and treatment of iron deficiency.

Research Gaps

- Assessing presence of anemia alone will miss the initial stages of iron deficiency.
- The evidence reviewed predominantly included nutrition-specific interventions in apparently healthy populations. Studies are needed on the effect of these interventions in high-risk populations like children with acute or chronic infections, acquired bone marrow disorders, inflammation or inherited anemia.
- Studies on Hb response in iron replete individuals that receive iron interventions should also be determined to look for any adverse effects with iron supplementation.

e. Standardising Hb Measurement

There is a clear variation in the Hb concentration assessed using capillary and venous samples [13,14]. In laboratory settings, automated analyzers should be preferred for measuring Hb. Non-invasive and invasive point-of-care analysers which are considered feasible for field settings due to portability and lower cost, have variable comparability to the reference. Harmonized, evidence-based guidelines validating the use of venous blood and standardization of automated analysers will have a positive impact on health equity and will ensure same definition of anemia is applied to all.

Monitoring and Evaluation of Implementation of Guidelines

An efficient system for the routine collection of relevant data, including relevant determinants of health, therapeutic adherence, and measures of programme performance, is critical determinant to ensure achievement of the right to health for all population groups. The impact can be evaluated within individual countries on national or regional scale or can be assessed across countries (i.e. adoption and adaptation of the guideline globally), implemented through different program initiatives of WHO.

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Table I Hemoglobin (g/dL) Cutoffs in the 2001 Versus 2024 WHO Guidelines for Diagnosing Anemia

| Population | 2011 Guidelines | 2024 Guidelines | Mild | Moderate | Severe |
|---|-----------------|------------------------|---------|----------|--------|
| Children (6-23 months) | <110 | < 105 | 95-104 | 70-94 | < 70 |
| Children (24-59 months) | <110 | < 110 | 100-109 | 70-99 | < 70 |
| Children (5-11 years) | <115 | < 115 | 110-114 | 80-109 | < 80 |
| Children (12-14years, non-pregnant girls) | <120 | < 120 | 110-119 | 80-109 | < 80 |
| Children (12-14 years, boys) | <120 | < 120 | 110-119 | 80-109 | < 80 |
| Adults (15-65 years, non-pregnant girls) | <120 | < 120 | 110-119 | 80-109 | < 80 |
| Adults (15-65 years, men) | <130 | < 130 | 110-129 | 80-109 | < 80 |
| Pregnant women | <110 | First trimester < 110 | 100-109 | 70-99 | < 70 |
| | | Second trimester < 105 | 95-104 | 70-94 | < 70 |
| | | Third trimester < 110 | 100-109 | 70-99 | < 70 |

Table II. Hemoglobin Adjustment for External Factors

| | <i>Recommendations</i> | <i>Research Gaps</i> |
|---------------------------------|--|--|
| Residence elevation | WHO recommends to adjust Hb levels as per elevation to diagnose anemia | <ul style="list-style-type: none"> Variations in populations living in elevated areas (>2500m) across the world Variations in Hb differences in children versus adults living in elevated areas |
| Infection/inflammation | No adjustment in Hb as vast differences in the origins and severities of infection and inflammation. | Need for improved accuracy and field-friendly measurement of inflammation |
| Genetic ancestry/ethnicity/race | Hb concentrations should not be adjusted due to insufficient evidence and complexity of operationalization | Further research on single nucleotide polymorphisms in iron or Hb regulation and further studies of the genetic basis for ethnic differences in iron metabolism are needed. |

Hb Hemoglobin

Table III Adjustments in Hemoglobin Concentration (g/L) for Every 500m Increment in Elevation [11]

| <i>Elevation range (meters above sea level)</i> | <i>Adjustments in Hemoglobin concentration^a (g/L)</i> |
|---|--|
| 1-499 | 0 |
| 500-999 | 4 |
| 1000-1499 | 8 |
| 1500-1999 | 11 |
| 2000-2499 | 14 |
| 2500-2999 | 18 |
| 3000-3499 | 21 |
| 3500-3999 | 25 |
| 4000-4499 | 29 |
| 4500-4999 | 33 |

Adjustments are the amount subtracted from an individual's observed Hb level or added to the Hb cutoff defining anemia (in g/L).

^aProposed adjustments for all population groups based on the equation: Hb adjustment (g/L) = (0.0056384 x elevation) + (0.0000003 x elevation²).