



Addressing the challenges of anaemia in the Andean region

Executive Summary

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Anaemia affects more than 1.5 billion people globally. It has disproportionate impacts in low- and middle-income countries and on vulnerable populations such as children, women of reproductive age and pregnant women. As well as short-term harms, its effects on child development have long-term implications for health and economic wellbeing.

Anaemia results from an insufficiency of red blood cells needed to deliver oxygen to meet the metabolic needs of all the body's tissues. There are many possible causes of inadequate red blood cell number, including lack of iron, a component of oxygen-carrying haemoglobin in red blood cells. Indeed, low haemoglobin levels are generally used as an indicator of anaemia and the condition is frequently treated by iron supplementation.

However, it is likely that around half of all cases of anaemia are not caused by iron deficiency, but by alternative factors such as infection or inflammation, which can limit iron availability for red blood cell production, or by other causes unrelated to iron. Since iron supplementation has the potential to have harmful impacts, there is growing interest in ensuring it is used appropriately for those with identified iron deficiency or at high risk of deficiency.

In addition, a growing understanding of iron metabolism and iron homeostasis is providing new insights into how anaemia can be triggered. In particular, research has highlighted the pivotal role of a liver peptide, hepcidin, as the master regulator of iron metabolism. In Andean regions, physiological adaptations to high-altitude living and low oxygen levels add further complexity to the regulation of iron and the development of anaemia.

In the 1960s, the World Health Organization (WHO) developed guidelines for the diagnosis of anaemia based on haemoglobin levels. These included adjustments for factors such as age and sex, but also took into account the fact that haemoglobin levels vary with altitude. However, little work has been done to validate these thresholds among people living at high altitude, leading to concerns that anaemia is being over-diagnosed in these populations. This could be exposing populations to unnecessary and potentially harmful interventions, and also diverting resources away from other important public health challenges.

In January 2021, the UK Academy of Medical Sciences and the National Academy of Sciences, Peru, jointly organised a two-day workshop to discuss these issues. Through plenary presentations and breakout sessions, workshop participants identified a range of priority research questions that need to be answered to ensure a more evidence-based approach to the challenge of anaemia in the region.

Causes and contributory factors: Participants identified a need to gain a deeper understanding of how distal risk factors (such as poverty) and proximal risk factors (such as nutrition, infections, inflammation and hypoxia) interact to influence the risk of anaemia at

high altitude. A key question is around the proportion of cases that are due to iron deficiency and are therefore theoretically treatable through iron supplementation.

Mechanisms of iron homeostasis and anaemia: More information is needed on iron metabolism in high-altitude Andean populations, as well as on how other factors such as iron sequestration related to infection influence the risk of anaemia. Other important questions include how iron metabolism changes in such populations with age and at key stages of life such as pregnancy, and the implications this has for the risk of anaemia.

Diagnosis of iron deficiency: If haemoglobin levels are still to be used to diagnose anaemia, there is a need to identify more appropriate thresholds to diagnose iron deficiency in Andean populations. Haemoglobin is a poor indicator of iron status, since there are other causes of low haemoglobin concentration, and individuals may be iron deficient without being anaemic. More appropriate thresholds need to be developed and validated across different age groups in high-altitude populations.

There is also the potential to incorporate specific markers of iron status (such as ferritin and hepcidin, accounting for the confounding effect of inflammation) into diagnostic criteria; new approaches such as dried blood spot analysis could be developed for harder to reach populations.

Consequences of anaemia: Participants identified a need to determine whether functional readouts might replace or complement use of haemoglobin testing in the diagnosis of anaemia. A better understanding of the consequences of mild anaemia at altitude would help to determine whether interventions are necessary in this group. More information is needed on the impact of anaemia on vulnerable populations, such as pregnant women at high altitude, and on the consequences of anaemia in pregnancy on the life-long health of offspring and their susceptibility to disease.

Treatment and prevention: Participants discussed the need to identify the most appropriate dosing schedules given new knowledge of iron homeostasis, as well as the potential for alternative treatment approaches such as intravenous iron administration. More information is also needed on the potential detrimental effects of iron supplementation on the gut microbiome. Multiple practical questions remain to be answered, including the relative advantages of supplements and fortification of foodstuffs, the best sources of iron for interventions, and the key factors underpinning the effectiveness of intervention programmes. Furthermore, treatment approaches not focused on iron should also be evaluated, in particular identifying and addressing causes of inflammation.

Methodologies: A range of approaches that could be taken to address these questions were identified. They included analysis of data from routine health and demographic surveys, as well as in-depth studies of risk factors in high-altitude populations, including phenotypic and genotypic studies of iron metabolism in the context of high-altitude hypoxia. Collaborations – both within the Andean region, and with other high-altitude areas – were seen as important to generate comparative data. Engagement with communities was identified as vital to secure support for research and to ensure that communities have an opportunity to shape research studies.

Anaemia is one of the world's greatest public health challenges, but the extent to which it affects Andean populations is uncertain, as are its causes. Given the potential direct and indirect harms associated with unnecessary treatment, it is essential that ways are found to provide a clearer picture of the levels, causes and consequences of anaemia at high altitude, the need for treatment, and the best ways to deliver such treatment.



Academy of Medical Sciences
41 Portland Place
London, W1B 1QH
+44(0)20 3141 3200

info@acmedsci.ac.uk
www.acmedsci.ac.uk

 [@acmedsci](https://twitter.com/acmedsci)

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