

Chapter 3

Assessment of the prevalence and the nature of iron deficiency for populations: the utility of comparing haemoglobin distributions

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Summary

Even though there are a number of well established haematologic and biochemical tests to assess iron status, it is not always feasible to perform them under field conditions, especially in developing countries. Also, in such regions, factors other than poor iron intake, such as infections and hereditary disorders affecting red cell production, can interfere with the interpretation of iron-related tests. To overcome these limitations, we propose a simplified approach to assess iron status using only results from haemoglobin testing. The strategy of this approach is based on the observation that the most common reason for iron deficiency, poor dietary intake, has a differential impact on the iron status of children, women, and men. Whereas other factors affecting iron and haematological status lack such differential impact. This approach requires the comparison of haemoglobin distributions of children, women, and men from a specific population against their respective standard distributions (free from iron deficiency). Examples of populations with different factors contributing to iron deficiency from the Middle East, Africa, the Caribbean, and Alaska are used to illustrate this approach. The improved capacity of field testing for haemoglobin in recent years means more opportunity of assessing iron deficiency in countries when it is not always feasible to conduct the more comprehensive surveys using multiple iron tests.

Introduction

Several haematologic and biochemical tests are well established for screening or diagnosis of iron deficiency in individuals as well as for population-based assessment¹. Even

though the purpose of population-based assessment of iron deficiency differs from the purpose of screening individuals, the desirable features of the assessments overlap. The three common reasons for population-based or public health based application are: (1) characterization of the

extent and nature of iron deficiency in communities; (2) planning and design for appropriate intervention programmes; and (3) monitoring and evaluation for the effects of programmes.

Issues related to the use of indicators for population-based assessment

As is true for all clinical tests, the most important features for a test designed to assess iron deficiency in an individual is adequate sensitivity, specificity and, the positive predictive value for this particular disorder. Although these are also desirable features for tests used in population-based assessment², the more important features are the feasibility of carrying out the assessment, and ability to compare with findings over time or across populations. One feature of using indicators for population-based assessment is that tests of limited value for individual-based assessment can still be useful in characterizing a population. One good example is the use of anaemia as a proxy of iron deficiency when anaemia may not be adequate for assessing iron status for an individual. This is because there are several conditions other than iron deficiency that can cause anaemia. Nevertheless, anaemia can serve as a useful indicator of iron deficiency in a population, because a population with overall high prevalence of anaemia is likely to have overall high prevalence of iron deficiency. Using an indicator for population-based assessment is analogous to estimating the size of an iceberg by measuring the tip of iceberg above the water. Anaemia can be viewed as the tip of the iceberg for iron deficiency.

In using an indicator to define the prevalence of the condition of interest, it is common to apply a cut-off point to the laboratory values for individual-based screening. For example, for haemoglobin <11.0 g/dl is a commonly used cutoff to define anaemia for young children who require further clinical evaluation, and it is also used for population-based assessment. One drawback of this approach is the tendency to regard only individuals with laboratory values below or above the cutoff as affected, and to focus intervention on those who meet the definition for the indicator, when in fact a much

greater proportion of the population is affected. This is like using the tip of an iceberg to define the size of the iceberg without taking into account the larger portion underwater. One way to bypass this pitfall is to present the entire distribution of the laboratory findings against a reference or standard distribution which is free from iron deficiency. The proper application of the prevalence of an indicator based on a laboratory cut-off point is to view the prevalence as an index of severity; interpretation of this index requires knowledge from previous studies and the background of the populations.

Assessment of iron deficiency

Three options exist for assessing the status of iron nutrition in dietary iron intake assessment: use of single haematologic or biochemical test, and use of multiple biochemical tests. By far, anaemia as a single indicator is the most commonly used approach to assess iron status of a population. There are, however, limitations with this approach if not taken into account in the interpretation of the findings: (1) anaemia is not specific for iron deficiency in some parts of the world; (2) anaemia represents a more severe form of iron deficiency; and (3) anaemia may not have adequate predictor value for iron deficiency when iron deficiency is mild or when the prevalence for a population is low. To avoid some of these limitations and the common misapplication of the prevalence of anaemia as the proportion of the population affected by iron deficiency, we propose the use of the entire haemoglobin distribution.

Use of dietary intake of iron

Assessment of the dietary intake of iron is an indirect approach for estimating the status of iron nutrition. The main advantage of this approach is that, with proper training and procedures, it is not difficult to collect information on the quantity of food consumed and the frequency of consumption. Use of this method is highly feasible because it does not require laboratory procedures. Unfortunately, this technique has several limitations. Although study results indicate that the assessment of a relatively simple dietary pattern of infant feeding has a strong predictive value for the risk of iron deficiency in young children³, studies in adults

have shown a lack of correlation between estimated dietary iron intake and iron nutrition status. Assessment of dietary intake in infants is a useful approach because the majority of the diet is milk-based, so the iron content of the milk is the main determinant of iron status⁴. The poor correlation for adult dietary iron content and iron nutrition status is partly due to common use of a method that estimates the total dietary iron content, and which often fails to take into account the bioavailability of iron in food items and the fact that other dietary components can increase or decrease the absorption of iron⁵. Another reason that dietary iron assessment is of limited value, particularly in industrialized countries, is that, for women, menstrual blood loss that is higher than average is a major determinant of iron deficiency, a factor that appears to be more important than dietary iron intake.

Given the indirectness and limitations of dietary assessment for iron nutrition status, the most important role of dietary iron assessment is to complement the information on iron nutrition status that is based on laboratory assessment. This information can be helpful in defining the programme content of the food-based approaches that have potential to improve iron nutrition. Investigators can use dietary assessment as adjunct information in determining iron nutrition status. They can collect this information by using qualitative approaches as part of the effort to understand the nature of iron deficiency.

Use of single haematologic or biochemical test

A survey based on haemoglobin or haematocrit measurements to define the prevalence of anaemia in a population is the most common approach for assessing the extent of iron deficiency. There is good evidence to support the assumption that, in many parts of the world, iron deficiency is the predominant cause of anaemia. Operationally, because haemoglobin measurement is one of the most commonly performed laboratory tests worldwide, it is often feasible to obtain measurements of haemoglobin or haematocrit. The common approach of measuring the prevalence of anaemia for the maternal and child health population is useful

for defining the severity of iron deficiency in a population. In a later section an expanded approach, comparing the entire haemoglobin distribution with reference distributions, will be described with several examples.

No single biochemical tests other than haemoglobin or haematocrit is commonly used to define iron nutrition status in a population. It is possible that serum ferritin levels could be used as an indicator of iron deficiency because low serum ferritin reflects low iron stores in the body is a more specific indicator for iron deficiency. High serum ferritin levels could also be used as an indicator for populations in which iron overload is a concern. In developed countries where iron deficiency anaemia is relatively uncommon, haemoglobin levels and/or anaemia are less sensitive in detecting variations in iron nutrition status among populations. Unlike serum ferritin which has no upper biological limit, the upper value of haemoglobin is regulated by tissue oxygen requirements which do not increase with increasing body iron load beyond what is sufficient for an optimal level.

Use of multiple biochemistry tests

Each of the well-known biochemical tests for iron reflects a different aspect of iron metabolism. Often, application of multiple tests for the same individual gives inconsistent results⁶. This problem has led to the development of a strategy to characterize nutrition iron status using multiple iron tests to define iron deficiency. This approach was developed for the assessment of iron status of the US population based on the National Health and Nutrition Examination Surveys (NHANES)^{7,8}.

The principle of applying multiple tests in parallel is that the certainty of iron deficiency increases with the increase of the number of abnormal tests. For the NHANES-based assessment, iron deficiency was defined as having abnormal results in two or more of three iron-related tests. Two models of multiple tests were used in the NHANES study: (1) the ferritin model, which uses the tests for serum ferritin, transferrin saturation, and erythrocyte protoporphyrin; and (2) the MCV model which uses the tests for mean corpuscular volume (MCV), transferrin saturation, and erythrocyte protopor-

phyrin⁷. There are two advantages of using multiple tests to define iron deficiency: (1) multiple indices allow differentiation of the severity of iron deficiency and; (2) this approach can be useful even when iron deficiency is not a common problem, as is the case in the USA.

However, the use of multiple tests has several disadvantages. The most obvious one is that the approach is relatively costly and operationally complex, and is thus not very feasible for a large-scale survey work in many parts of the world. It is also an approach mainly suited for use in more developed settings, where iron deficiency is often an isolated finding. In many less developed areas, high rates of infection or inflammatory conditions and other nutrient deficiencies impede the determination of iron deficiency in the population (because such conditions can interfere with biochemical tests for iron); the more recently developed transferrin receptor test is an exception^{9,10}. The lack of agreement on cut-off points and standardized methods for some of the tests makes comparison of survey findings difficult. The use of multiple tests to assess iron nutrition status appears to be more suited for clinical studies based of well-defined population samples in limited locations than for large-scale population-based assessment.

Expanded use of the haemoglobin test

In addition to cost, feasibility and the appropriateness and limitations of different approaches with which to assess iron deficiency, several

factors affect the choice of an assessment method. It is important to determine the cause(s) of anaemia and iron deficiency in a given population. Possible causes include decreased bioavailability of dietary iron, blood loss related to hookworm, infections that can interfere with iron metabolism, and nutritional deficiency other than iron such as vitamin A or folate deficiencies. Development of an assessment approach that would provide information and clues regarding cause(s) of anaemia and iron deficiency would be helpful. Because the risk of iron deficiency differs for children, women, and men in most populations, all these three groups need to be assessed. This method is based on the general knowledge of the causes of iron deficiency in relation to different stage of economic development and ecological conditions¹¹. Table 1 summarizes the general risk for iron deficiency for subpopulations of children, women, and men for areas at different stages of economic development - less developed, intermediate and developed.

In recent years, there has been improvement in the feasibility of conducting haemoglobin testing for populations in remote field settings, related to the availability of a new-generation haemoglobin photometer, the HaemoCue (Angelholm, Sweden). The HaemoCue photometer is battery operated and uses a dry reagent (sodium azide) in a microcuvette for direct blood collection and measurement. The portability and stability of this system has made it more feasible to measure haemoglobin in

Table 1. Risk for iron deficiency and anaemia for subpopulations in areas with different stages of economic development

Stage of economic development	Children	Women	Men
Developed	Low: Iron fortified diet available Moderate: Lack of iron fortified diet	Low: Mainly for subset with excessive menstrual blood loss	None
Intermediate	Moderate to high: Lack of iron fortified diet	Moderate: Low iron bioavailability	None to low
Less developed	High: Lack of iron fortified diet and low iron bioavailability of supplementary food	High: Possibility that other factors in addition to iron deficiency contribute to anemia	Low: Not affected by hookworm Moderate: affected by hookworm

remote field settings without formal laboratory support. The accuracy and precision of haemoglobin values based on HaemoCue are comparable to those of the standard laboratory method¹². All of the major case examples of haemoglobin distributions from different countries presented here were based on the HaemoCue system.

The extent and the nature of iron deficiency in different situations

Developed countries - adequate dietary iron intake and moderate iron deficiency

In industrialized societies, where dietary iron intake and bioavailability are relatively high, the modest level of iron deficiency anaemia is observed mainly in young children and women of childbearing age. A good example is a finding from the US national surveys (NHANES^{7,8}). Young children are at greater risk of iron deficiency than older children and adults because rapid growth during infancy results in a relatively high requirement for iron⁴. In addition, the amount of iron in the infant diet is generally not adequate to meet iron requirements unless the diet is fortified with iron³. The relative lack of overlap in the dietary intake of infants and adults can put young children at risk for iron deficiency, even in countries where the adult diet is adequate in iron content and bioavailability. Data from studies conducted in Argentina, Canada and the United States support this proposition¹³⁻¹⁵.

Women of childbearing age are at greater risk of iron deficiency than men because the average blood loss of 40-50 ml at each menstrual cycle increases their requirement for iron to an average 50 per cent higher than that for men¹⁶. For a small subset of women who have high menstrual blood loss exceeding 80 to 100 ml per cycle, it is difficult to meet their iron requirement with a diet that is otherwise adequate for most women. For this reason, in developed countries it is fair to assume that the primary cause of iron deficiency is menstrual blood rather than lack of iron content or lack of bioavailability of iron in the general diet. Studies have established that, in such a setting it is possible to observe a modest level of iron defi-

ciency anaemia in young children and women of childbearing age but not in men^{7,8}.

Anaemia is not specific for iron deficiency in an individual especially when the prevalence is low. Also, because iron deficiency anaemia represents the more severe form of iron deficiency, not all individuals with iron deficiency have anaemia. Nevertheless, monitoring the prevalence of anaemia can still be a useful approach to determining iron deficiency in a population. The reduction of childhood anaemia in response to improved infant iron nutrition in the United States is an example of the usefulness of this approach^{15,17}. (Fig. 1)

The NHANES are the few sources of broad population-based assessment in which multiple tests for iron were used. Consequently, we are able to use the NHANES data to characterize the optimal haemoglobin distribution to serve as a reference that can be helpful in assessing iron status for other populations. An optimal haemoglobin distribution can be defined after excluding the subset of the sample with biochemical evidence of iron deficiency (two or more of the three tests in the MCV model). Figure 2 illustrates the optimal haemoglobin levels for children under 5 years age, and for women and men 18-44 years of age in the USA. The distinct and generalized difference in haemoglobin distributions for children, women and men is the basis for applying age- and sex-specific criteria in defining anaemia.

Figure 3 shows the haemoglobin distribution for the 10 per cent in the women in the United States who had evidence of iron deficiency based on having two or more abnormal test for iron (the MCV model). This distribution is compared with that for the 90 per cent of the women who were regarded as non-iron deficient. The iron deficient group have a generalized downward shift if their haemoglobin distribution in contrast to the non-deficient group, but the overlap between the two distributions is substantial. This overlap suggests that the haemoglobin test has limited usefulness for detection of milder forms of iron deficiency because many subjects with iron deficiency have haemoglobin values above the standard cutoff point for anaemia of 12.0 g/dl for women.

From the perspective of population-based assessment, a modest downward shift of the entire haemoglobin distribution, as shown in Fig. 3, indicates that most if not all of the subjects had lower haemoglobin levels. This finding suggests that such a comparison of haemoglobin distribution can avoid the common pitfall of regarding only subjects with anaemia as iron deficient. Several examples are given later to further demonstrate the limitations of haemoglobin testing for detecting individuals with iron deficiency. However, this limitation does not negate the usefulness of haemoglobin testing for population-based assessment.

One major complication of using haemoglobin testing to assess iron deficiency is the need to apply appropriate criteria for reference. The haemoglobin distribution used for assessment of anaemia in a population is commonly adjusted for sex and age. Other non-pathological factors that can cause shifting of the haemoglobin distribution are altitude and pregnancy¹⁸. There is also increasing evidence that some races or ethnic groups may have distinct haemoglobin distributions that are independent of iron nutrition status¹⁹. Figure 4 shows a comparison of haemo-

globin distributions for non-iron deficient black and white women based on the NHANES II data. If the same criteria for anaemia were used, the number of black women classified as anaemic would be three times the number of white women considered to be anaemic. For this reason, in using the haemoglobin test to define iron status, a reference haemoglobin distribution based on black subjects would be the appropriate reference for comparison with a population that was mainly of African extraction.

Areas with intermediate developments - low dietary iron intake or poor bioavailability as major cause of iron deficiency anaemia

In many parts of the world where economic development can be regarded as being at an intermediate stage, iron deficiency anaemia is quite common mainly among children and women. These areas include most of South and Central America, the Middle East, North Africa, and the northern part of Asia. In these regions anaemia is mainly due to poor bioavailability of dietary iron because of low intake of meat which contains the more bioavailable form of haem iron, and greater exposure to inhibitors of non-haem

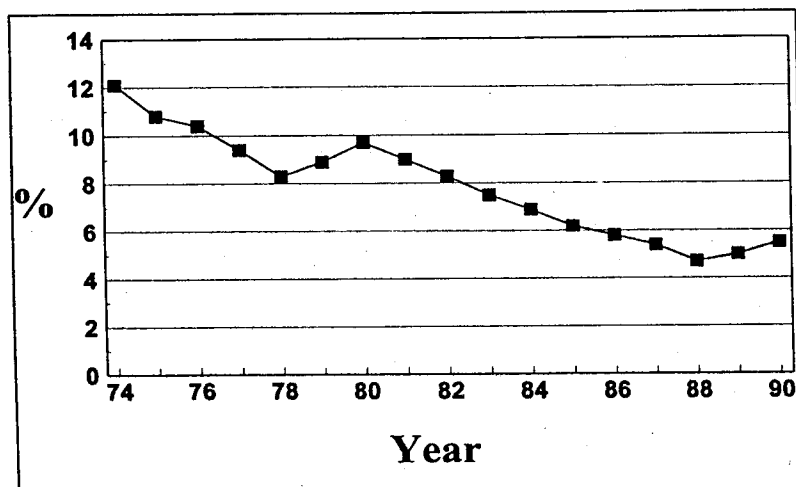


Fig. 1. This finding demonstrates that the prevalence of anaemia is a useful tool for the population-based monitoring of iron deficiency. Graph showing declining trend of anaemia in low income families in the United States. This trend reflects improved iron nutrition status. The improvement was related to a significant change in the iron content of the infant diet during the same time period¹⁵.

Fig. 2. Graph showing distribution of haemoglobin levels for children aged 1 to 5 years and women and men aged 18 to 44 years. Data are from National Health and Nutritional Examination Surveys II, after exclusion of individuals with abnormal values for mean corpuscular volume (MCV), transferrin saturation and erythrocyte protoporphyrin. These distributions are used as a standard for comparison with haemoglobin distributions from other surveys.

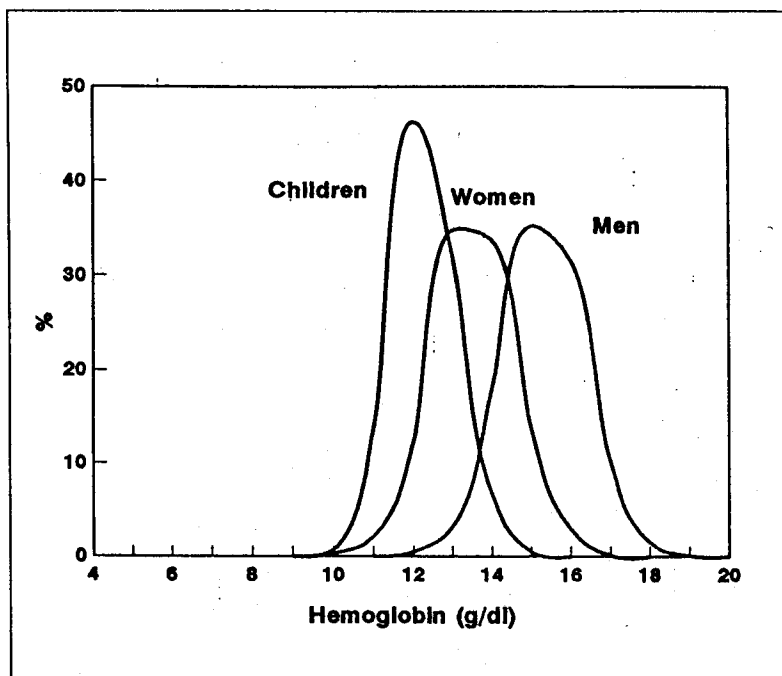
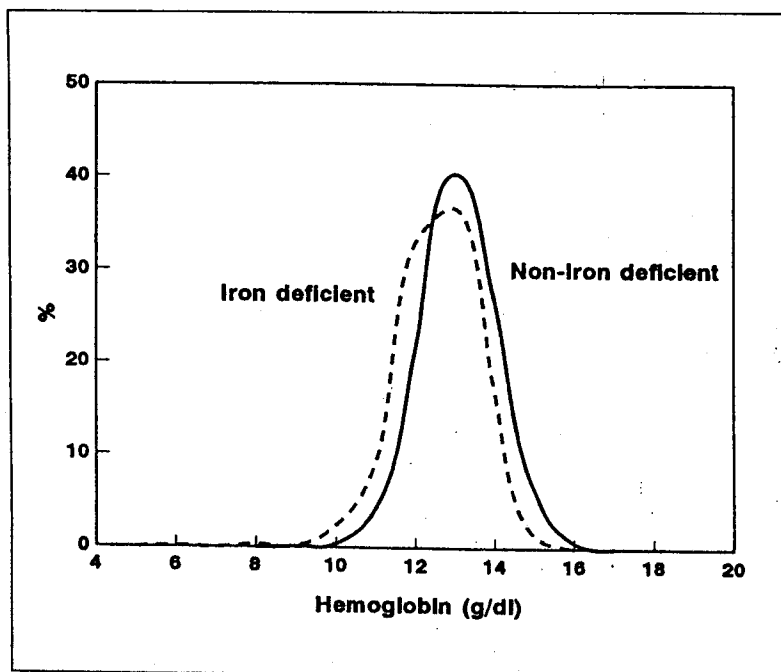


Fig. 3. Graph showing a comparison of the optimal haemoglobin distribution for women who were not iron deficient in NHANES II with the distribution for women who had abnormal results in two or more tests for iron nutrition. The women with iron deficiency made up approximately 10 per cent of the women in the USA. Haemoglobin values for women who had iron deficiency were lower than those for women who had no iron deficiency. Data are from the US National Health and Nutritional Examination Surveys (NHANES II).



iron absorption, such as phytate in grain and tannic acid in tea. In these areas other major causes of anaemia, such as malaria or iron deficiency related to gastrointestinal blood loss due to hookworm, are rare or the condition is mild. Except for instances of greater severity or higher prevalence, the pattern of anaemia is similar to the pattern for developed countries in that it mainly affects young children and women. This finding indicates that when low dietary content or poor bioavailability of iron is the main reason for iron deficiency, the prevalence or severity of anaemia can be used as an index of iron nutrition status.

The Middle East is a region where, for the most part, poor iron intake is the major cause of anaemia. Figure 5 shows the haemoglobin distributions for children, women, and men of the Palestinian refugees residing in Syria, Jordan, Lebanon, the West Bank and Gaza, using the optimal or the non-iron deficient haemoglobin distribution based on the US sample (NHANES II) as a comparison¹¹. The Palestinian refugees did not have an adequate source of iron in the infant diet; consumption of meat is relatively

low because of low socioeconomic status; and tea consumption is common and starts in late infancy. Comparison of the distributions shown in Fig. 5 indicates that the prevalence of anaemia is relatively high for Palestinian children and women, as indicated by a substantial downward shift in haemoglobin distribution. The distribution for Palestinian men is not very different from that for men in the USA. This finding indicates that even when iron intake is grossly inadequate for children and women, men still do not suffer from significant iron deficiency. The marked shift of haemoglobin distribution for children and women indicates that most of them were affected by iron deficiency, not just those below the common anaemia cut-offs.

Another example is based on the national iron deficiency survey of Grenada for which, in addition to haemoglobin testing, serum ferritin level was also determined. Analysis of this survey confirms that a similar differential shift of haemoglobin distribution between women and men, as observed in the Middle East, is indeed the result of iron deficiency. In Grenada, where

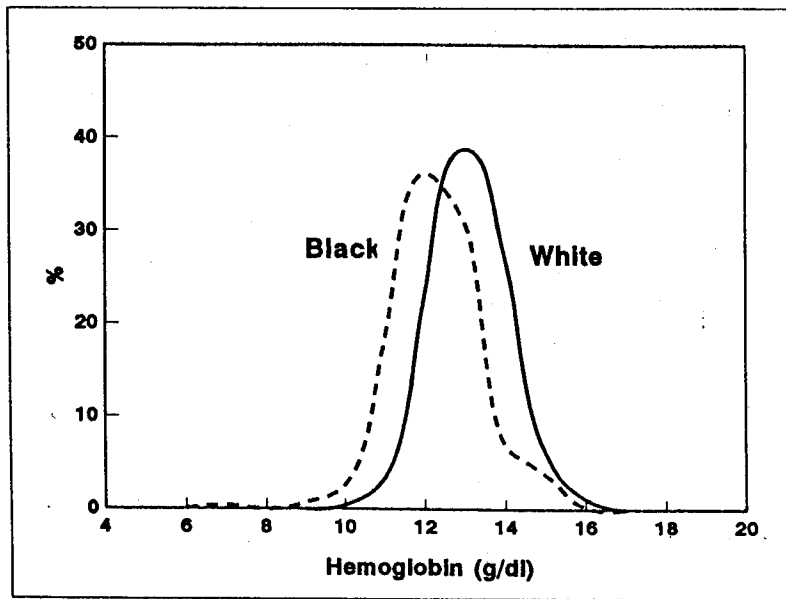


Fig. 4. Graph showing comparison of haemoglobin distributions for black women and white women who were not iron deficient. Haemoglobin values for black women were lower than those for white women. Data are from the US National Health and Nutritional Examination (NHANES II).

there is little problem with hookworm infection or malaria, poor iron intake or low iron bioavailability is the only plausible explanation for iron deficiency anaemia observed. Their haemoglobin distribution for men is similar to that for non-iron deficient black men in the USA (Fig. 6a). Haemoglobin levels for Grenadian women were substantially lower than those for non-iron deficient US black women (Fig. 6b). This finding suggests high rates of iron deficiency in Grenadian women.

However, when only the small subset of non-iron deficient Grenadian women (serum ferritin levels $\geq 30 \mu\text{g/l}$) was retained, their haemoglobin distribution was found to be similar to that for non-iron deficient US black women (Fig. 6c). This finding clearly indicates that the marked shift of haemoglobin distribution for the entire sample of Grenada women was mainly related to iron deficiency. That few Grenadian men had a low serum ferritin level confirms our

impression that it is possible for men in a population to have little or no iron deficiency, even when women in the same population have substantial iron deficiency.

On the basis of these two examples, a case can be made that inclusion of adult men in an anaemia survey can yield information that will be useful in determining the nature of iron deficiency in women and children.

Less developed countries - causes of anaemia in addition to low dietary iron intake

From the point of view of economic development, by far the most challenging areas for assessing iron nutrition status are the less developed countries that comprise a substantial part of sub-Saharan Africa and South and Southeast Asia. In these regions, beyond poor dietary intake of iron contributes to the common and severe iron deficiency observed, hookworm infection often plays a major role by causing

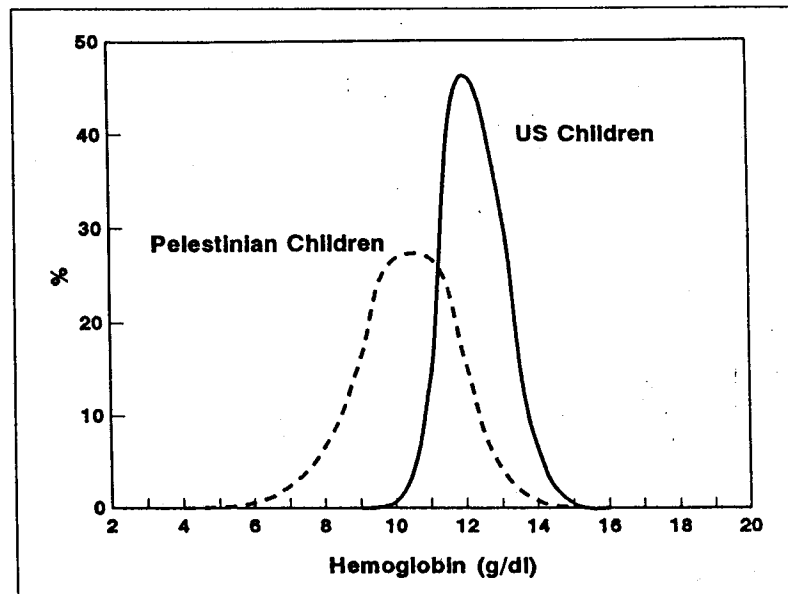


Fig. 5. Graphs showing lower haemoglobin levels for Palestinian children (Fig. 5a above), women (Fig. 5b), and men (Fig. 5c) than for children, women and men in the US population. The Palestinian refugees residing in five areas in the Middle East were surveyed in 1990. Haemoglobin levels in this population were mainly affected by low iron intake and poor bioavailability of dietary iron. There were no other major causes for anaemia or blood loss. Haemoglobin distributions indicated substantial iron deficiency in children and women but not men¹¹.

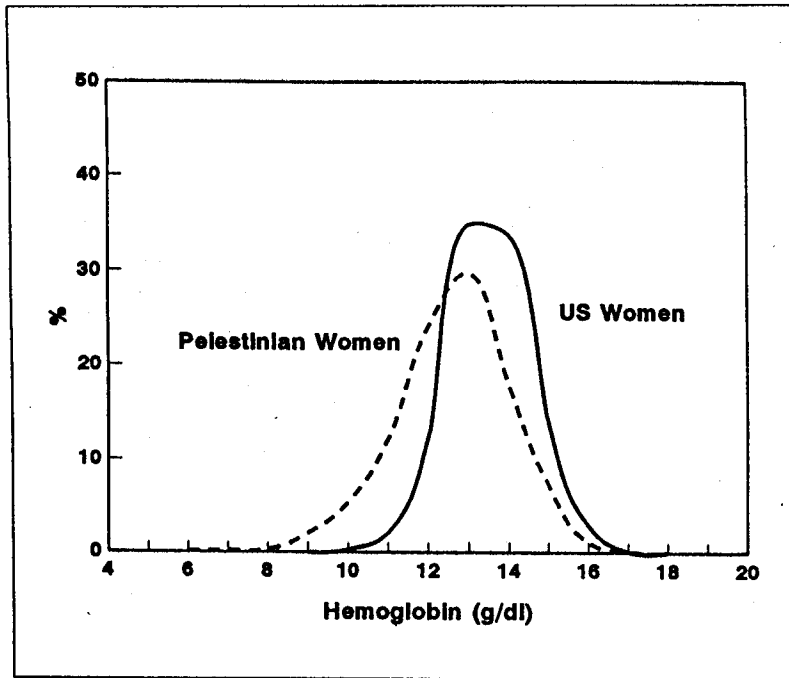


Fig. 5b

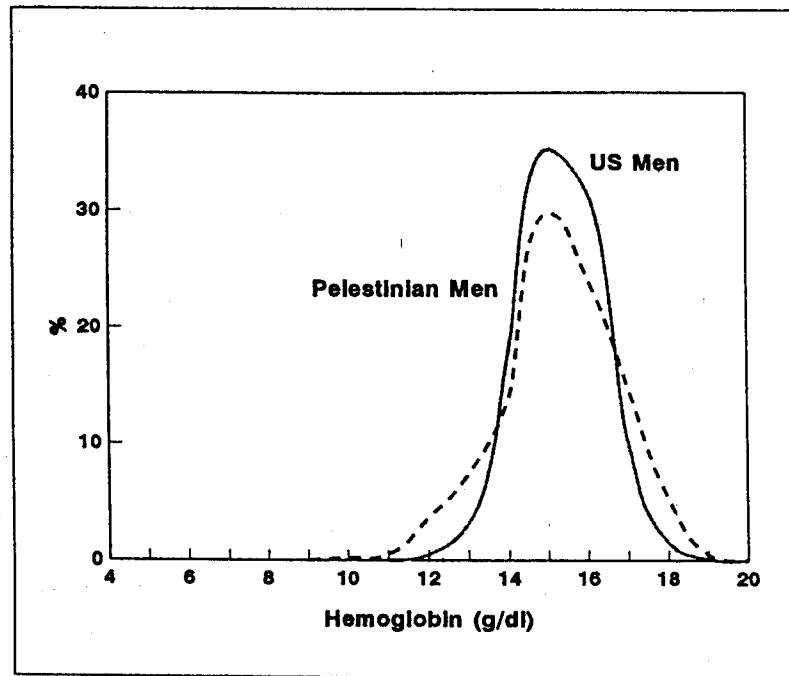


Fig. 5c

clinically significant gastrointestinal (GI) blood loss²⁰. Factors other than iron deficiency contributing to anaemia is also common: infections include malaria and hereditary haemoglobinopathies and defects in red blood cell production. All these conditions render the use of haemoglobin levels for assessing iron deficiency difficult. Unfortunately, the use of biochemical tests for iron is not an alternative because infections and inflammatory conditions can affect iron metabolism and make it difficult to interpret most tests for determining levels of iron. In less developed countries, it is also less feasible to implement biochemical tests for population-based or large-scale assessment. Despite its limitations, haemoglobin testing appears to be the most viable option for assessment of iron deficiency in the populations of the less developed countries.

The finding of a high prevalence of anaemia or low haemoglobin levels for children and women in less developed countries is to be expected. The finding that men also have anaemia requires other forms of evaluation in order to determine the likely cause of the anaemia. One major possibility is that men are iron deficient and hookworm infection is a likely cause in many tropical areas. The proper determination of the intensity of hookworm infection is to perform limited stool examination for hookworm egg counts. In the case of malaria or nutritional deficiency as possibilities for the high rates of anaemia among men, assessment of haemoglobin response during therapeutic trials for subjects with anaemia may be the best approach for defining the nature of the anaemia. In a recent study of combined vitamin A and iron supplementation for pregnant women with anaemia

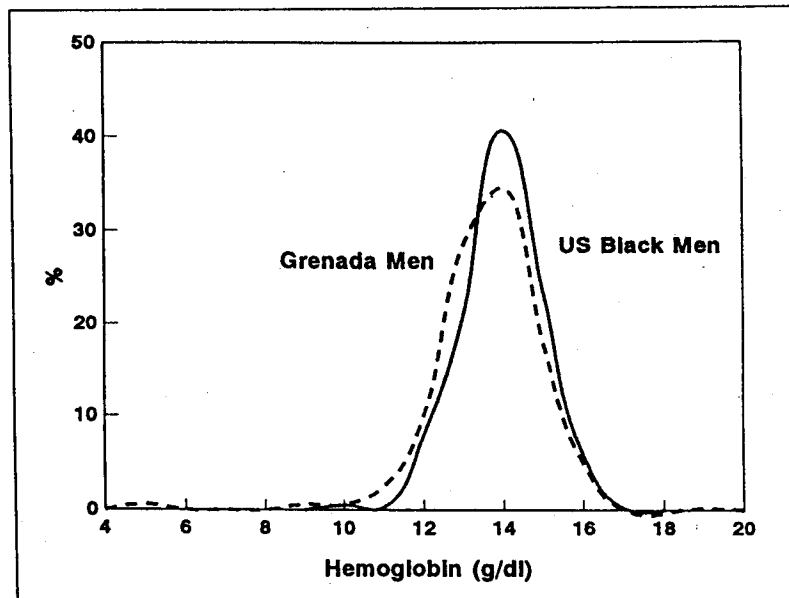


Fig. 6. Graphs showing comparisons for haemoglobin distributions for Grenadian men versus that for black men in the United States. (Fig. 6a, above), and for Grenadian women versus black women with no iron deficiency (Fig. 6b). Haemoglobin levels for Grenadian women were substantially lower than those for black women in the USA (Fig. 6b). This finding indicates high rates of iron deficiency for Grenadian women. For Grenadian women with serum ferritin levels $\geq 30 \mu\text{g/ml}$, who made up less than half of the total sample of women, the haemoglobin distribution is similar to that for black women in the USA who were not iron deficient (Fig. 6c). This finding indicates that the shift of haemoglobin distribution for the entire sample of women was mainly related to iron deficiency.

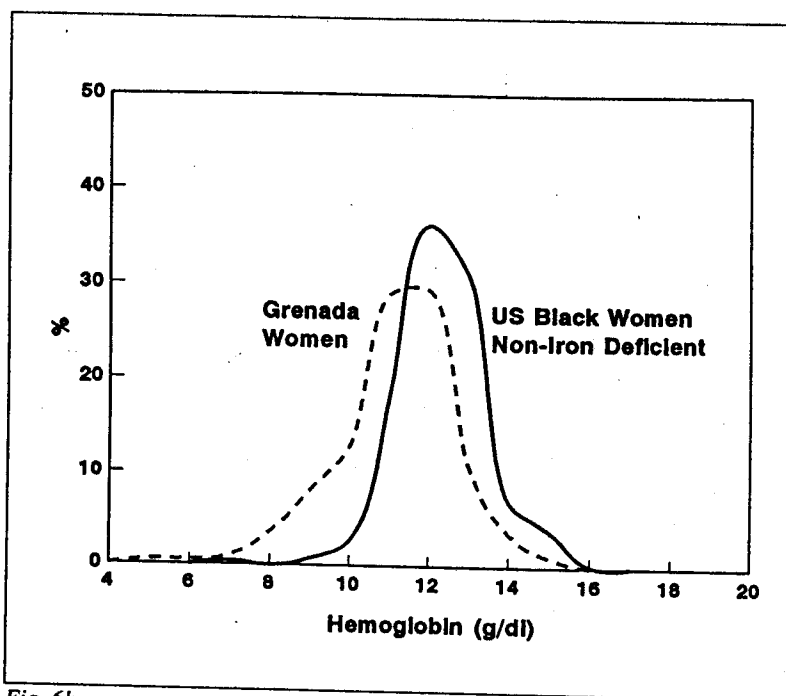


Fig. 6b

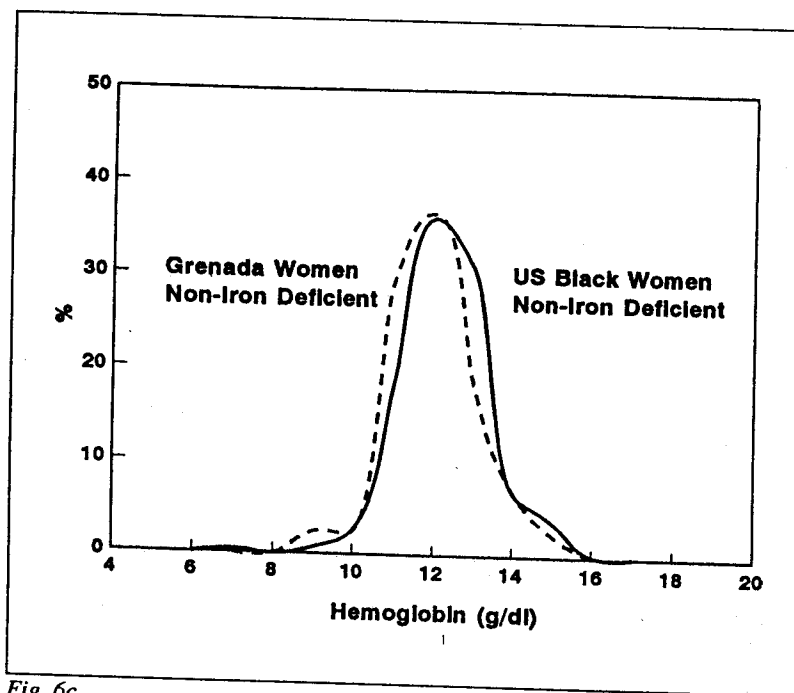


Fig. 6c

Table 2. Proportion of pregnant women with anaemia responding to dietary supplements with increase in haemoglobin to ≥ 11.0 g/dl)*.

Treatment	No of patients	Response (%)	95% Confidence interval
Placebo	62	16	7-29
Vitamin A only	63	35	22-48
Iron	63	60	54-79
Iron and vitamin A	63	97	88-99

* Data from Suharno *et al.*²⁰

Table 3. Amount of blood loss estimated by quantitative stool haeme analysis and prevalence of anaemia for Zanzibar children with different hookworm loads^a

Hookworm infection degree of disease hookworm load (eggs/per gram of faeces)	No. of children	Mean faecal haemoglobin (mg/g of stool)	(%) With anaemia ^b
None 0	45	1.24	49
Light 1-9999	83	1.46	57
Moderate 2000-3999	19	2.96	68
Heavy ≥ 4000	56	8.79	80

^a Data from Stoltzfus *et al.*²²

^b Children were considered to have anaemia if haemoglobin levels were < 11.0 g/dl.

in Indonesia, investigators found that vitamin A deficiency together with iron deficiency contributed substantially to the high rates of anaemia observed²⁰ Table 2 details the response to vitamin A and iron supplementation for that study conducted by Suharno *et al.*

Example of areas with low dietary iron intake and common gastrointestinal blood loss

In the tropics hookworm infection with resulting iron deficiency is the most common epidemic form of blood loss anaemia; it affects mainly older children and adults^{20,21}. In a recent study of school-age children in Zanzibar, Stoltzfus *et al.* found a remarkable correlation between iron deficiency anaemia and GI blood loss related to hookworm infection using a quantitative method in determining faecal blood content (HaemoQuant) (Table 3). For the heavily infected children, the estimated daily blood loss was more than 5 ml²². Rates of anaemia ranged from 49 per cent for children without hookworm infection to 80 per cent for those

with heavy infection. The high rates of anaemia for those children without hookworm infections fit with the general impression of low iron intake in this population and were confirmed by serum ferritin testing.

Figure 7 shows comparisons of haemoglobin distributions for Zanzibar school-age children and adult men with those for black children and black men in the United States. The marked downward shift of haemoglobin distribution for men in Zanzibar suggests that they have substantial rates of anaemia due to GI blood loss related to hookworm infection. An unusual example of adequate dietary iron intake but increased gastrointestinal blood loss

Another example of common GI blood loss and iron deficiency affecting the haemoglobin distributions for both men and women is the recently discovered epidemic form of *Helicobacter pylori* gastritis in the Alaskan Eskimo natives in the Arctic region²³. Unlike the population affected by hookworm in the tropics,

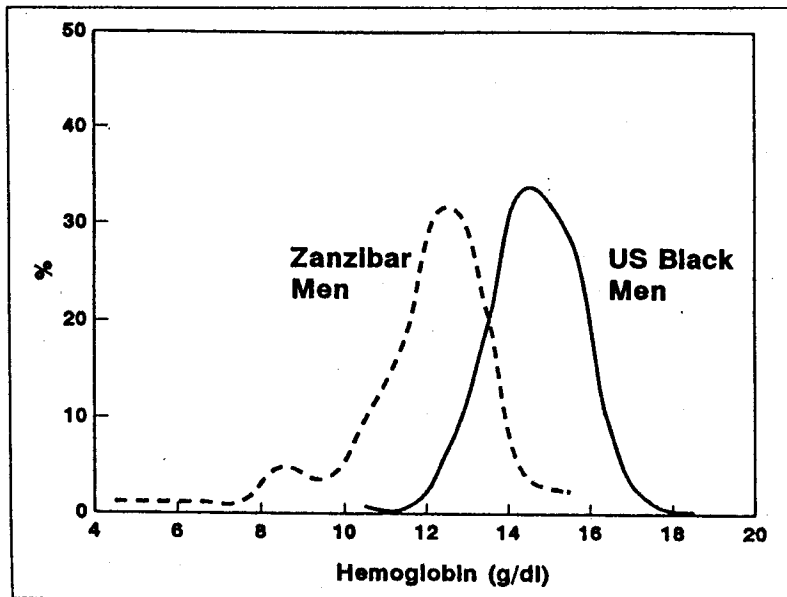
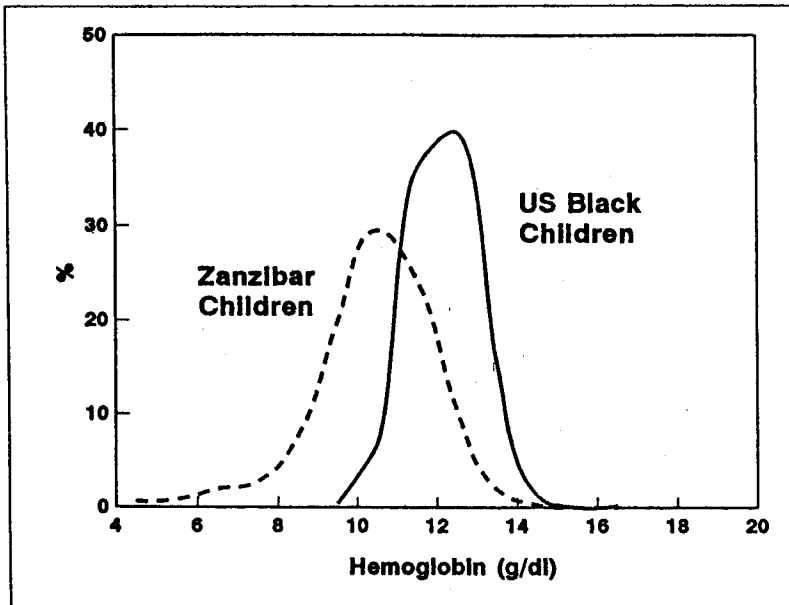


Fig. 7. Graphs showing comparisons of haemoglobin distributions for Zanzibar children (top), and Zanzibar men (bottom). Black children and black men with no iron deficiency, in the USA, are the reference. These comparisons indicate that hookworm infection and the resulting gastrointestinal blood loss is related to decreased haemoglobin levels. This finding suggests that the substantial rates of anaemia in the country are related to gastrointestinal blood loss due to infection with hookworm.

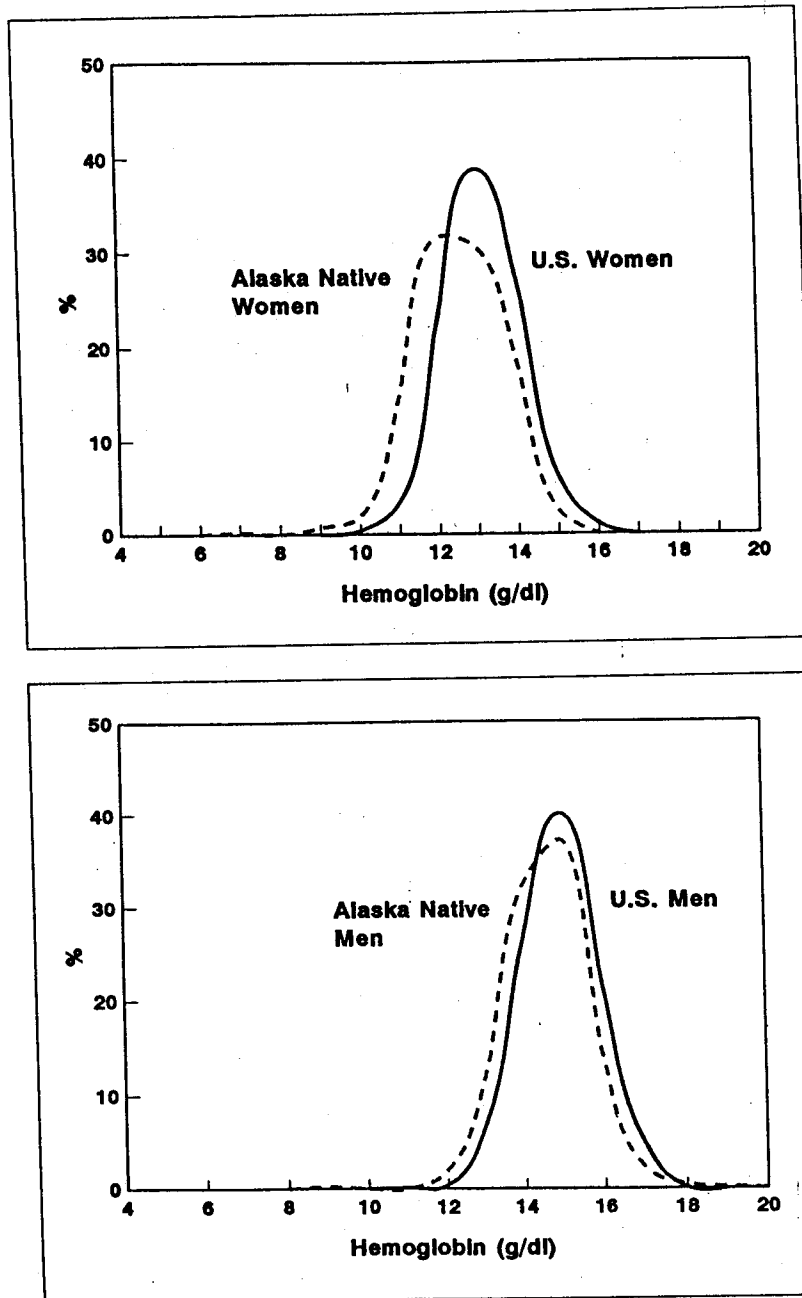


Fig. 8. Graphs showing comparisons of haemoglobin distribution for Alaskan Eskimo Native men (top) and women (bottom) versus those for men and women in the USA. These results show a modest trend toward lower haemoglobin levels for both Alaskan men and women, because of iron deficiency related to increased gastrointestinal blood loss due to an atypical presentation. *Helicobacter pylori* gastritis is common in the Arctic region. The iron deficiency is not severe because dietary iron intake is adequate in this population.

where iron intake is generally low, Alaskan Eskimos have adequate iron intake with rich sources of haem iron from fish and land and marine mammals²⁴. The increased occult GI bleeding due to gastritis resulted in lower iron stores and thus prevalence of iron deficiency for both men and women that were higher than those for men, and women in the US general population²⁵.

Figure 8 shows comparisons between the haemoglobin distributions for Alaskan Eskimo men and women against the optimal distributions based on the US sample. In contrast to the optimal distribution, the Alaskan men had a slightly but generalized lower haemoglobin distribution suggesting many of them were affected by iron deficiency. This is confirmed by the fact that the Alaskan men had a median serum ferritin level of 31 g/ml in contrast to the value of 132 µg/ml for men in the USA. This finding indicates that when iron deficiency anaemia is relatively mild or the prevalence is not high, serum ferritin can better differentiate the iron nutrition status of populations. The main constraint against using serum ferritin level as an indicator of iron deficiency is the lack of a field test, which limits its use for large-scale surveys.

The two examples from Zanzibar and Alaska support the proposition that it is useful to examine the haemoglobin distribution or prevalence of anaemia for men. This approach can be helpful in differentiating iron deficiency that

is mainly due to low iron intake or to excessive blood loss. For this reason, the addition of a sample of men should be considered for anaemia surveys which usually focus only on maternal and child populations.

Conclusions

The predictive value of haemoglobin testing is limited when screening individuals for iron deficiency in areas where prevalence of iron deficiency is low, but haemoglobin testing can be useful for population-based monitoring. The comparison between haemoglobin distributions for children, women, and men and respective standard distributions can provide valuable diagnostic information concerning the cause of iron deficiency in the population. In areas with multiple causes of anaemia, the use of treatment response may be the only alternative for determining the nature of anaemia other than iron deficiency. The proposed approach of comparing haemoglobin distributions or prevalence of anaemia against standard distributions for children, women and men has the potential for increasing the feasibility of iron deficiency assessment in countries where it is not always feasible to conduct comprehensive surveys by using multiple tests for iron. In developed countries where iron deficiency is mild and iron overload is a concern, the use of serum ferritin levels to monitor iron nutrition status should also be considered.

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