ANAEMIA A MONITORING TOOL FOR HELMINTH INFECTION

Abstract

Helminthic infections also known as worm infections affect mostly the gastrointestinal tracts.They are caused by parasites known as helminths. The infection is capable of causing blood loss which often leads to anaemia. However the severity of anaemia is dependent on the intensity of the infection.With an estimated 3.5 billion infected individuals globally, helminth infections are among the most prevalent infections. In tropical and subtropical regions, these infections primarily affect the most impoverished and disadvantaged communities that have limited access to clean water, sanitation, and hygiene. The highest prevalence of these infections has been reported from sub-Saharan Africa, China, and South America. The major helminths that causes anaemia includes Hook worm (Necator. americanus and Anclystoma. duodunale) , Ascarislumbricoides, Trichuristrichuria (whip worm).Hookworms and whipworms are examples of helminths that cause iron-deficiency anemia through blood consumption and by causing damage to the intestinal mucosa during feeding.It is estimated that adult hookworms consume 0.05 to 0.2 milliliters of blood per day per worm, with an average daily blood loss of 26.4 milliliters in adult subjects infected with A. Duodenale. There are many risk factors which can lead to acquiring these infections and they include eating raw or undercooked meat and fish, poor hygiene, inadequate availability of clean water, poor sanitation. Some of the symptoms includes blood loss, abdominal pain ,vomitting .Helminth infection can be diagnosed through direct wet mount, concentration technique and stool sample is used for this diagnosis.Helminth infections can be treated using antihelminthic drugs. Helminths can be prevented through safe sanitary facilites,maintainance of personal hygiene mass deworming in the affected areas and health education. In conclusion a well developed medical health care system should be put in place to control the devastating effects helminths infections.

Keywords*: helminthic, infection, gastrointestinal tract, wormanaemia*

Introduction

The gastrointestinal tracts are the primary target of helminthic infections, commonly referred to as worm infections. They are brought on by helminth parasites. Blood loss from the infection can occur, and this frequently results in anaemia. Nonetheless, the degree of the infection determines how severe the anaemia is. Anaemia is a major tropical disease nowadays and a global issue. There have been reports of severe iron-deficiency anaemia from South America, Africa, and

India [1]. Even though there are many possible causes of these anaemia's, it is now clear that chronic blood loss brought on by specific helminthic and parasitic infections is a major contributing factor to their genesis [2].

Helminthes are classified into two major phyla [3.4]. Whereas the platyhelminths, also referred to as flatworms, include the flukes, also referred to as trematodes, such as schistosomes, and the tapeworms, also referred to as cestodes, such as the pork tapeworm that causes cysticercosis, the nematodes, also known as roundworms, include the major intestinal worms, also known as soil-transmitted helminths, and the filarial worms that cause lymphatic filariasis (LF) and onchocerciasis [3, 4].

According to Muñoz-Antoli*et al.* (2018), helminth infections affect roughly one-third of the nearly three billion people who survive on less than two US dollars per day in developing regions of sub-Saharan Africa, Asia, and the Americas [5.6]. Ascariasis, Trichuriasis, intestinal helminth infections, and hookworm infections are the most common causes of helminthiases; lymphatic filariasis and schistosomiasis are the next most common infections. In real terms, this implies that the people living in thousands of remote, underdeveloped villages across the tropics and subtropics are frequently chronically infected with multiple parasitic worm species; in other words, they are polyparasitized[6]

A common disease in many tropical and semitropical nations is hookworm. Infected are more than 450 million people. Ancylostoma duodenale infection is found in up to 29% of patients admitted to Egypt's Endemic Disease Hospitals, and hookworm infection is the primary cause of severe iron-deficiency anemia in farmers [7].

Schistosomiasis affects more than 100 million people worldwide, and this figure may rise as new irrigation projects are implemented in many developing nations. Africa, the Middle East, South America, the West Indies, and the Far East are all home to schistosomiasis. More than 70% of Egyptian farmers have schistosomiasis, and according to Farid's review of the etiology of anemia in Egypt, schistosomiasis-related anemia is the most common in Egyptian patients, while ancylostomiasis-related anemia is the most severe [3, 5]

As a result, a significant portion of this discussion will focus on defining the role played by common helminthic infections in causing blood loss and iron-deficiency anemia. Recently, significant progress has been made in quantifying the relationship between the intensity of parasitic infection, anemia, and blood loss (González [8]. The helminths that cause chronic blood loss from the urinary system or gastrointestinal tract are linked to iron-deficiency anemia. These include schistosomiasis (Schistosoma mansoni, S. haematobium, and S. japonicum), whipworm infection (Trichuris trichiura), and hookworm infection (Necator americanus and Ancylostoma duodenale) [8].

Epidemiology of Anaemia causing Helminth Infections

Helminths do not reproduce in the human host, with the exception of Strongyloidesstercoralis[3, 4,9] This basic feature of helminth biology establishes a set of dynamics for transmission that are very different from those of bacteria, fungi, viruses, and protozoa. For instance, because morbidity is linked to the number of worms infecting the host (i.e., the worm burden) rather than the presence or absence of infection, prevalence which is the percentage of individuals in a defined population at a given time point is rarely used as the only metric to evaluate the epidemiological situation for that helminth infection. Worm burden, also known as the "intensity of infection," is frequently combined with prevalence. For intestinal helminths and schistosomes, worm burden is commonly measured by the number of eggs per gram (EPGs) of feces. The WHO divides people into three infection categories: light, moderate, and heavy based on EPGs and their correlation with morbidity. Moreover, the WHO advises using both infection frequency and intensity to categorize communities into three transmission categories for soil-transmitted helminths: category I (high), category II (medium), and category III (low) [4,6.9].These transmission categories are assigned based on the prevalence of infection (greater or less than 50%) as well as the number of community members who are heavily infected (greater or less than 10%). A community would be classified as a category II transmission community, for instance, if its prevalence was higher than 50% but its heavy infection rate was lower than 10% [3, 5.9]Helminth infection prevalence globally is estimated to be 1.5 billion, *Ascaris lumbricoides* (roundworm*)* prevalently reported if Africa. Asia and Latin America is estimated to be between 807–1121 Million . Hookworms (*Ancylostoma duodenale* and *Necator americanus*) is reported to be 576–740 million especially in improvished countries of Asia and Africa In addition *Trichuris trichiura* and Strongyloidesstercoralis is estimated to have a prevalence of 604–795 million and 30 – 100 million respectively especially in developing countries [**9.10**]. It is reported that over 236 million people are infected with schistosomiasis requiring preventive treatment [**11**]. *Taenia* spp. or *Hymenolepis nana* are estimated to infect 95 to 135 million people globally [**12,13]**

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Association of Helminth Infection intensity withAnaemia

Helminth infection is associated with low hemoglobin level and increased risk of anemia[14.]Anaemiacan be brought on directly by blood loss or indirectly by inflammation, hypersplenism, anorexia, bone marrow suppression, or hemolysis. People Infected with *S. mansoni*, hookworms, *E. vermicularis*, and *Taenia* spp. infections. are more likely to suffer from anemia [3.10]. Even mild infections greatly increase the risk of anemia. The amount of blood lost from hookworm infections (*Necator americanus* and *Ancylostoma duodenale*) is highly and linearly correlated with worm load and faecal egg count. In addition to causing intestinal blood loss, *Trichuris trichiura* also increases the risk of anemia (haemoglobin [Hb] <11 g/dl) in school-aged children infected with the virus compared to uninfected controls [3, 5.11].

Worm diseases are a major cause of mild and moderate anemia (i.e., Hb 7–11.9 g/dl) in communities where transmission is high. For instance, anemia affects 50%–62% of Tanzanian children and 66% of pregnant Tanzanian women who live in high-risk areas for helminth and/or schistosomiasis infections. Blood loss from the intestines or urine is caused by *Schistosoma mansoni, S. japonicum, and S. haematobium*[12,15]. Research from Kenya, Niger, Tanzania, and other countries has demonstrated that, even in the presence of confounding variables, the egg count in *S. mansoni* and S. haematobium is negatively correlated with the hemoglobin levels of children and expectant mothers. In tropical nations, polyparasitism which is the simultaneous infection with multiple parasites is prevalent, especially in impoverished areas [3,12,16]. The quantity of parasites in an infected individual and their Hb level are inversely correlated. For instance, the prevalence of anemia (Hb<11 g/dl) is five times more common in children in the Philippines who have low-intensity polyparasite infections. Eight-fold increases in anemia are linked to moderate-to-high intensity infections with three or four soil-transmitted helminths and S. japonicum [13.17].

Apart from its application in specific worm disease programs, anemia monitoring may also prove to be a valuable instrument in the integration of helminthiasis control with other major illnesses. When co-infections with helminthiasis and malaria, HIV, and/or tuberculosis occur, anemia is a major cause of morbidity. Malaria is the cause of up to 35% of anemia cases in African children [12,18].Anaemia contributes to the progression of both HIV and tuberculosis and is an independent prognostic marker in HIV infection. In certain instances, reversing anemia can lower the risk of dying young from HIV-related complications [11,17].

Aetiology of Helminths Causing Anaemia

Common worm infections are the primary parasites that cause blood loss in humans and directly result in iron-deficiency anemia. These include schistosomiasis *(Schistosoma mansoni, S. haematobium, and S. japonicum*), whipworm infection (*Trichuris trichuiria*), and hookworm infection (*Necator americanus and Ancylostoma duodenale*). Molla and Mamo (2018) identified *Strongyloidesstercolaris* [4,6,10].

Hookworm

A N. Americanus infection can result in more than one milliliter of blood loss per day. By consuming blood and harming the intestinal mucosa during feeding, helminths like whipworms (*Trichuris trichiura*) and hookworms (*Necator americanus and Ancylostoma duodenale*) can cause iron-deficiency anemia. Adult subjects infected with *A. duodenale* have an average daily blood loss of 26.4 ml. Adult hookworm *N. americanus and A. duodenale* are thought to ingest 0.05 to 0.2 ml of blood per worm per day. According to reports from Brazil, China, Mexico, India, the United States, Mauritius, Egypt, and Venezuela, there was a corresponding drop in hemoglobin concentration as hookworm infection loads increased [4, 7,11].

A quantitative relationship between the degree of anemia (measured by hemoglobin concentration per 100 ml of blood), actual blood loss, and the intensity of hookworm infection (measured by counting all worms passed after treatment) was finally established with the introduction of the chromium 51-red blood cell-tagging technique for the measurement of intestinal blood loss [3,4,10] According to studies using radioisotope techniques, patients suffering from a heavy hookworm infection may lose up to 29 mg of iron in the gastrointestinal tract and 250 ml, or a quarter of a liter, of blood every day [11,17].

It has recently been demonstrated that intestinal protein loss in patients with severe hookworm infection may lower the total serum proteins, particularly the serum albumin. Severe hookworm infection and anemia are frequently associated with edema and hypoalbuminemia [3, 4,9].

With several helminthic infections, a malabsorption syndrome that resembles tropical sprue has been reported to occur. Studies indicate that patients with heavy hookworm infections have impaired folic acid absorption even though they are unable to show any malabsorption of vitamin B12 [13,19]Furthermore, it has been documented that patients with severe hookworm infection have low serum vitamin B12 and folic acid levels. It's unclear if these low levels resulted from loss, malabsorption, or dietary deficiencies [4,13,19].

Trichuiristrichuria

Children with severe infections had red cell losses ranging from 0.8 to 8.6 ml/day.Consequently, it can be said that childhood anemia can be caused by infections with more than 800 parasites [4, 5]. An estimated 800 million infections occur worldwide due to the parasite Trichuris trichiura, also known as whipworm, which causes trichuriasis, which is often asymptomatic. A serious infection in children is most likely to result in malnourishment and possibly anemia. The worms can cause diarrhea and pain in the abdomen if they multiply too much.In the feces, unembryonated eggs are passed. Before the eggs embryonate and become infectious, they go through two stages of development in the environment. After eating the infectious eggs, the larvae are released, grow into adults, settle in the colon, and adhere to the mucosa. The worm can pierce and embed its whip-like anterior portion into the intestinal wall of the host thanks to a spear-like projection. The eggs that the female worms produce are eventually expelled in the stool [14,20].

(Trichuris trichiura), by consuming blood and causing harm to the intestinal mucosa during feeding, contribute to iron-deficiency anemia.It has been calculated that each worm infected with Trichuris trichria loses about 0.005 milliliters of blood per day [14,20].

Schistosomiasis

A study that used red blood cells tagged with Chromium 51 documented blood loss in two patients who had colonic and rectal polyps and later validated these findings in an additional ten patients. They stressed that while the average daily blood loss of 12.5 ml and iron loss of 3.3 mg might not be significant or result in overt anemia, they can definitely cause the body's iron reserves to be depleted [15,21]. The significance of the fact that, in certain geographic regions, helminthic infections other than hookworm may cause chronic intestinal blood loss was emphasized by these authors [15,21].

S. haematobium

In a study, urinary blood loss in eight *S. haematobium*-infected patients was measured using in vivo59Fe-labeled red blood cells. The results showed a loss ranging from 0.44 to 6.0 ml/day. Using the same methodology, Kim, Suh, and Hyun (2020) measured the urinary blood loss in nine patients who had severe hematuria and an infection with *S. haematobium*. The results showed that the daily mean iron loss ranged from 0.6 to 37.3 mg and that the blood loss varied from 2.6 to 126 mI/day [16,22]. They pointed out that while a *S. haematobium* infection can cause severe urinary blood loss, this loss typically occurs suddenly and is not continuous like it would be with a hookworm infection [16,22].

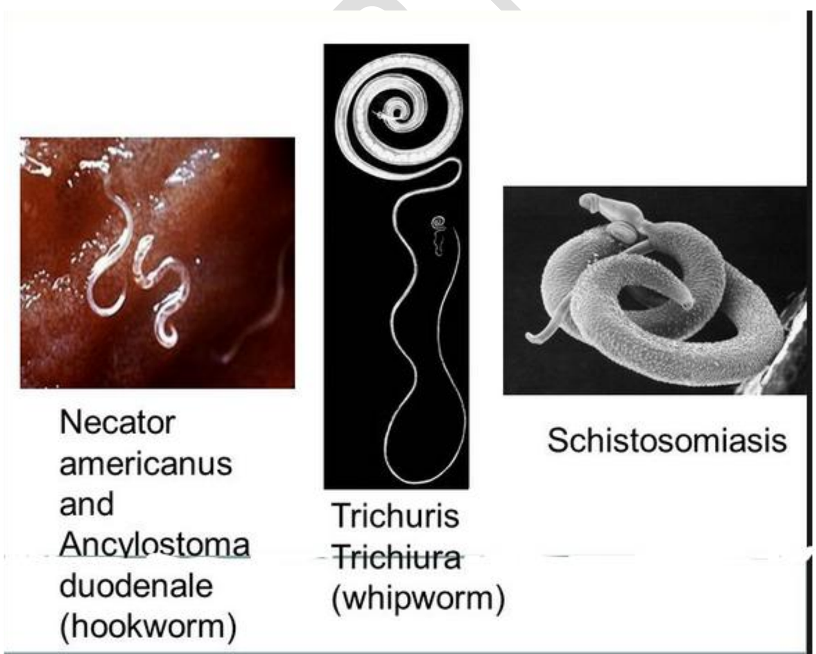

Fig 1: Hookworm, whip worm and Schistosoma

(https://www.cdc.gov/dpdx/diagnosticprocedures/stool/morphcomp.html)

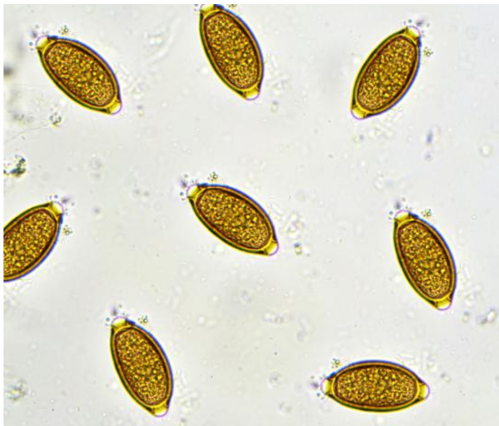

***Fig 2 :Trichuristrichuira* egg**

(https://www.healthline.com/health/digestive-health/pros-cons-colon-cleanse#risks)

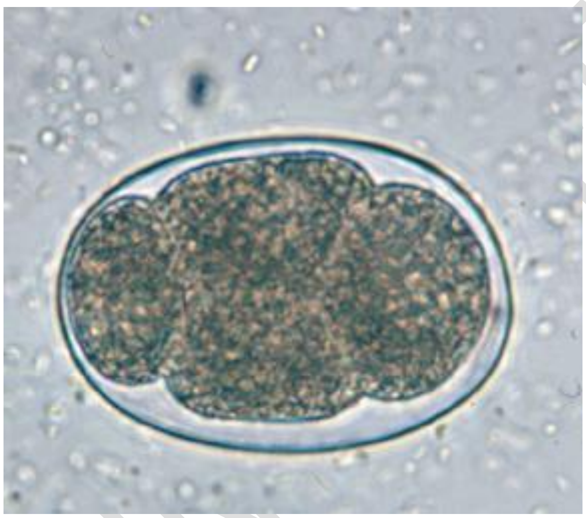

Fig3: Hookworm egg

Fig4: OVA OF SCHISTOSOMA SPECIES

https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/schistosoma

RISK FACTORS

In the end, human communities with high rates of poverty, poor hygiene, and a dearth of basic medical care are ideal environments for these helminth infections to flourish and endure. Intestinal parasite infections are global endemic diseases and are the leading cause of illness worldwide . The parasites are regarded as the major health problem in developing countries especially in children . Infection results in anemia, retarded growth, and impaired cognitive development and are classified among the major causes of absenteeism and daily adjusted years lost [17,23].

The majority of soil-transmitted helminth infections are found in low- and middle-income nations with inadequate sanitation and hygiene. Age, immunity, and the number of worms present in an infected individual are all factors that affect morbidity and mortality from STH infections. Sub-Saharan Africa, South Asia, China, Latin America, and China have the highest rates of infections with soil-transmitted nematodes [17,23].

In warm, tropical climates with a high prevalence of soil-transmitted helminths, the excretion of parasitic eggs from infected individuals contaminates the soil. Because the eggs passed in the feces need time to mature in the soil before they become infectious, there is no direct person-to-person transmission or infection from fresh feces. Reinfection only happens when these worms come into contact with an infectious stage in the environment because they do not reproduce within their human hosts [17,23].

Laboratory diagnosis

Helminthiasis, in both endemic and traveler populations, could be mild and remain unrecognized in some or misdiagnosed in others in spite of its severe clinical outcomes hence standard laboratory procedures should be employed in diagnosis of helminth infection, a few are mentioned below

Direct wet preparation

To identify helminth infections, such as those caused by the motile larvae of Strongyloidesstercoralis, direct microscopic examination of the feces is necessary. In most cases, it is also sufficient to identify elevated levels of Ascaris lumbricoides helminth infection eggs. This method's primary benefit is its speed and affordability. That is only semi-quantitative, though, and control programs don't typically use it. It entails emulsifying a tiny amount of fresh stool on a microscope glass slide in one saline drop. The emulsified stool is covered with a cover glass to create a thin smear preparation, which is then examined under a light microscope to look for parasite species' eggs, larvae, or trophozoites [24,25].

Kato-Katz technique

The WHO "gold standard" for determining the frequency and severity of STH infections is the Kato-Katz technique. Among the copro-microscopic techniques, Kato-Katz offers a number of benefits, such as high sensitivity, quantification of eggs, cost-effectiveness, and low infrastructure requirements. Using egg counts and cut-off values, infection intensities can be stratified. The sieved stool sample (roughly 41.7 mg, 20 mg, or 50 mg depending on the template size) is put on a glass slide for the Kato-Katz technique. Covering the preparation is a piece of glycerol-soaked cellophane. The slide is then turned inside out and gently pressed down to create a thin smear. The purpose of the additional glycerol is to "clear" the fat and fecal material surrounding the eggs. For hookworm eggs, this step takes roughly 30 minutes, but for other species, it can take anywhere from 1 to 24 hours to read the slide under a microscope. The number of eggs is then calculated under a microscope and expressed in terms of the number of feces per gram [14,25].

Formal –ether-concentration technique

In specialized laboratories, the formol-ether-concentration method is frequently employed to diagnose STHs. The primary benefit is its speed, which enables the concentration of various fecal parasites. This method works with both preserved and fresh excrement. By rendering the organisms inactive, formol reduces the possibility of contracting a fecal pathogen infection while in the laboratory. This method can be used to diagnose intestinal protozoa and STHs. Utilized in conjunction with the Kato-Katz technique, helminth diagnostic sensitivity is significantly increased. To enable sample storage and retrospective analyses, the stool samples can be fixed using diluted formalin or sodium acetate-acetic acid-formalin (SAF). A different method that makes use of acetone has been explained. Over time, the method has undergone a number of changes. The feces are first emulsified in formol water using the Ridley modified method, and then the suspension is strained to get rid of big fecal particles. The combined suspension is then centrifuged following the addition of ether or ethyl acetate. Fecal debris is suspended in the layer between the ether and the formol water, while parasitic elements, cysts, oocysts, eggs, or larvae are fixed and sedimented. To find and count the parasite, the entire sediment is further examined using a light microscope [14,25].

Flotation technique

The primary application of flotation tests is the identification of various parasitic worm eggs excreted in excrement. The lower specific gravity of the eggs in comparison to the flotation solutions (FS) is the basis for the fecal flotation of parasite eggs. Depending on the formulation, the different FS can have specific gravities ranging from 1.18 to 1.27. The majority of parasite eggs float because of their specific gravity (sg) of 1.05–1.20, whereas larger, denser fecal debris sinks to the bottom [1425].

Zinc sulphate flotation technique

This method works well for concentrating Giardia lamblia and Entamoeba histolytica cysts as well as Trichuris trichiura eggs. In comparison to other flotation techniques, it takes less time. The procedure uses a solution of zinc sulfate (sg: 1.180–1.200). To get rid of the fecal debris, one gram of feces is emulsified in tap water and strained. Following a centrifugation of the filtrate, the sediment is suspended in 4 milliliters of $ZnSO_4$ solution. The eggs and cyst are allowed to float to the top of the suspension by letting it stand for 30 to 45 minutes. To collect the eggs or larvae, a cover glass is placed over the tube. The eggs or larvae are then transferred onto a glass slide so they can be examined under a microscope [4, 24,25].

Treatments and preventions

Prevention

Helminth infections can be prevented by so many ways which includes the following ways:

- Wash your hands after using the restroom or touching dirt, as well as before consuming or preparing food.
- Mass deworming
- Carefully wash produce and fruits from your garden.
- Effective sewage disposal

- Not defecating outdoor
- Health education[26]

Treatment

Helminth infections can be treated with different antihelminthic drugs and these drugs includes the following:

1) Mebendazole
2) Praziquantel
3) Piperazine
4) pyrantel

Control and Management of Anaemia due to Soil Transmitted Helminthiasis

Recognizing the severity of the burden of helminth infection and associated anemia, WHO proposed several control measures which includes mass deworming to control infection with these parasites in a sustainable manner through existing health delivery channels This is the most effective method currently available to treat high-risk groups, especially school-age children, for STH infections is to regularly administer single-dose oral anthelminthic medications. According to the WHO intestinal helminth infections are the leading cause of disease burden among children in developing nations between the ages of 5 and 14 and are also highly controllable through cost-effective intervention.[9,10]

All intestinal infections, including those brought on by soil-transmitted helminthes (STHs), cannot be completely eradicated until every resident of endemic areas has access to culturally appropriate and efficient sanitation.

It is improbable that people in developing nations have access to sufficient sanitary facilities. Untreated human night soil, or feces, is mixed and applied as fertilizer to crops and vegetables throughout much of Asia, allowing infectious stages to enter the human food chain. The best available public health measure for managing soil-transmitted helminthes is the use of anthelminthic chemotherapy to reduce morbidity until sanitation improves significantly [10,11,25]. Re-infection will happen in the absence of sanitation, but medication use lowers intensity and consequently morbidity as well as the number of stages that are released into the environment.

In addition, the way children are treated in schools facilitates coverage, guarantees community compliance, and advances health education. Some of the evidence for these claims comes from work done in Nigeria, where A. lumbricoides was the helminth of special interest [9, 25]. Treatment strategies don't have to be limited to kids in school. Regular universal (mass) coverage might be the most economical course of action, and other community groups like expectant mothers might be the focus of care.[10,14]

Conclusion

The second most common cause of disability worldwide is anemia, which is addressed by a number of the global MDGs. For both helminthiasis and schistosomiasis, the relationship between anemia and worm infestation burden and control is well-established, and there are examples of these programs using population changes in haemoglobin levels as a monitoring tool.

However, worm infestations are frequently accompanied by iron deficiency, so these programs will only be able to slow down the rate at which hemoglobin is decreasing unless they include iron supplementation into their operations. Therefore, before these programs can consistently use anemia as a monitoring tool, a more precise relationship between the burden of other worm infestations and anemia needs to be established.

Anaemia should probably not be used as the only indicator because confounding factors affecting the aetiology of anemia, particularly dietary iron deficiency, will reduce its sensitivity and specificity. However, anemia could be a useful tool in the monitoring toolkit for worm infestations. As a result, drug distribution and compliance will probably continue to be the main instruments for program oversight. The inclusion of anemia in demographic health surveys and its significance as a health indicator in major nutrition, HIV, and malaria programs make hemoglobin monitoring useful for assessing other disease control initiatives.

Before anemia is strongly advised as a monitoring tool for worm infestation programs, a few questions need to be addressed. Although current worm infestation models are thought to be economical due to their low resource requirements, any extra activity, like measuring hemoglobin, runs the risk of overloading the system. Therefore, before preparing for scale-up, anemia as a monitoring tool needs to be carefully assessed in pilot projects and its cost-effectiveness determined. Carefully incorporating iron supplementation into worm infestation programs may improve their impact on anemia; however, this will have resource implications for currently cost-effective programs. For integrated worm infestation programs, cost-effectiveness data are available for the drug delivery components, but not for the other evaluation components. The effects of including haemoglobin measurements and potentially iron supplementation in current programs require more research.

Since it can precisely capture even the smallest variations in hemoglobin concentration, the HemoCue system is by far the most popular and widely recognized hemoglobin technology for worm infestation program evaluation. Additionally, the cost of the new HemoCueHb 301 tropical system is lower than that of the Hb 201 system. Although the HCS is easy to use and reasonably priced, it is not sensitive enough to detect even minute variations in hemoglobin to be used independently.

Combining the two systems—the HemoCueHb 301 for accurate measurements and quality control and the HCS (hemoglobin color sale) for mass screening—might be a smart move, though it hasn't been tested. It is vital to thoroughly standardize both methods, which can be achieved by routinely supervising and training staff members.Local differences in the frequency of worm infestations and anemia, as well as in the resources and technical know-how needed to implement and oversee worm infestation programs, are unavoidable.Therefore, any methods for determining the prevalence of anemia should be tested in real-world scenarios using predefined standards that come from the overall goals of the programs designed to eradicate worm infestations. Because it cannot be assumed that costs and effectiveness will remain constant as worm infestation programs are scaled up and reach more remote areas, this kind of evaluation is especially crucial.

Recommendation

Helminth infections continue to be a cause of significant morbidity and mortality in tropical and developing countries. Moreover, abundant evidence show these are a risk factor for anaemia. It is imperative that mass deworming programmes are instituted particularly in high-risk groups such as pre-school children and pregnant women so as to decrease the prevalence of anaemia in these cohorts.

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