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Anaemia in children: are we using the correct prevention strategies ?

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Introduction

Anaemia is defined as reduction of the haemoglobin concentration below normal levels [1]. Normal level of haemoglobin varies with age, sex, ethnicity and physiological states and is particularly variable during early childhood. Haemoglobin concentrations are high in new-borns (14.5-22.5g/dl) which drop rapidly, due to physiological reasons, over first two months of life to reach a nadir at 9-10g/dl. Haemoglobin level then stabilises above 11.0g/dl from 6-months onwards [1].

Anaemia is a long-standing public health problem among children across the globe. Prevalence of anaemia is highest in the African continent with extremely high rates (>60%) in sub-Saharan Africa. In most developing countries, prevalence of childhood anaemia ranges between 20%-60% [2]. The National Nutrition and Micronutrient Survey (2012) reported that the prevalence of anaemia among Sri Lankan children is 15.1%. Highest prevalence was in Kilinochchi district (26.9%) and lowest prevalence was in Kegalle district (4.9%) [3]. Younger children are more affected with highest prevalence reported in late infancy and second year of life.

Causes for anaemia are numerous. However, in asymptomatic children, anaemia is usually microcytic in morphology and is due to a limited number of aetiologies [4]. In Sri Lanka the leading causes for childhood anaemia are iron deficiency (ID) and haemoglobinopathy.

Iron deficiency anaemia

ID is still an important health problem in Sri Lanka. It is often seen in children below five years and is particularly problematic during late infancy and second year of life. According to a recent survey, the prevalence of iron deficiency anaemia (IDA) in Sri Lanka is 7.3% with district prevalence ranging between 3.0% (Batticaloa) to 12.9% (Killinochchi) (Table 1) [5]. Historically, anaemia in asymptomatic children was always attributed to IDA and Sinhalese term for anaemia – *'Rukthaheenathawa'* refers to both anaemia and ID [6]. This misconception is persistent among the public, medical doctors, administrators and policy makers. However, it is important to realise that all anaemias are not due to ID. In fact, the nutrition survey revealed that only 48% of children with anaemia are iron deficient [5].

Table 1. Prevalence of anaemia, iron deficiency anaemia and haemoglobinopathy by district (Combined data from National nutrition and micronutrient survey [3, 5] and Thalassaemia survey [7])

District	*Prevalence of anaemia*	*Prevalence of IDA*	*Prevalence of β-thalassaemia*	*Prevalence of α-thalassaemia trait*
Colombo*	17.1%	8%	0.6%	5.2%
Gampaha*	15.8%	10%	2.6%	7.2%
Kaluthara*	14.7%	7%	0.0%	6.4%
Kandy*	16.9%	9%	2.9%	6.0%
Matale	12.9%	8%	3.1%	5.5%
Nuwara-Eliya#	13.3%	4%	1.7%	8.7%
Galle*	8.9%	6%	1.0%	3.2%
Matara	10.0%	4%	1.3%	6.7%
Hambanthota	9.7%	6%	3.1%	4.5%
Rathnapura*	11.1%	6%	0.7%	5.0%
Kegalle#	4.9%	3%	2.6%	8.8%
Badulla	15.9%	6%	2.2%	4.8%
Moneragala	25.6%	10%	5.1%	6.9%
Batticaloa	15.3%	3%	2.6%	9.1%
Trincomalee	23.1%	8%	1.3%	8.5%
Ampara#	13.6%	6%	5.8%	8.3%
Killinochchi*	26.9%	13%	2.5%	6.5%
Mullathivu#	14.3%	4%	2.6%	7.8%
Jaffna	18.6%	7%	1.0%	6.9%
Vavuniya	18.1%	8%	1.7%	9.2%
Mannar	15.4%	8%	4.7%	9.6%
Kurunegala#	16.0%	6%	6.7%	14.0%
Puttlum	20.3%	12%	2.0%	11.7%
Anuradhapura#	16.2%	9%	10.0%	13.9%
Polonnaruwa*	21.5%	11%	2.2%	8.7%
Sri Lanka	**15.1%**	**7.3%**	**2.8%**	**8.0%**

* Districts in which the prevalence of iron deficiency anaemia are higher than haemoglobinopathy which could be identified as target areas for iron supplementation.

\# Districts in which prevalence of haemoglobinopathy is as twice that of iron deficiency anaemia. In these districts universal iron supplementation may be detrimental.

β-Thalassaemia

Next important cause of anaemia in Sri Lankan children is haemoglobinopathy [8]. Disorders of the β-globin which include β-thalassaemia, HbE disease and sickle cell disease are the most clinically significant haemoglobinopathies in Sri Lanka [9]. β-Thalassaemia major is due to homozygous or compound heterozygous mutations in the β-globin gene and is characterised by severe symptomatic anaemia which is invariably fatal without blood transfusions [10, 11]. Milder form of the disease which is due to heterozygous mutations of the β-globin gene is known as β-thalassaemia trait [12]. A recent island wide survey in Sri Lanka reported on the prevalence of β-thalassaemia trait (2.0%), HbE trait (0.5%), sickle cell trait (0.1%) and HbD trait (0.2%) [7]. Collectively this contributes to an overall prevalence of 2.8% of heterozygous β-globin mutations which accounts for approximately 19% of children with asymptomatic anaemia.

α-Thalassaemia

α-Thalassaemia has thus far, not been considered as a significant cause of anaemia in Sri Lanka. This is due to the rarity of clinically significant α-thalassaemia (haemoglobin H disease and Barts hydrops foetalis) in Sri Lanka and to technical difficulties in confirming α-thalassaemia trait which is only feasible through DNA analysis. However, a recent survey showed a high (8.0%) prevalence of α-thalassaemia trait [7]. Surprisingly, α-thalassaemia is more prevalent than beta-thalassaemia and IDA in many parts of the country (Table 1) [7]. In contrast to what was previously described, this data suggests, that haemoglobinopathy rather than ID is the likely cause of anaemia in a significant proportion of children.

Hook worm infestations

Hook worm (*Necator americanus*) infestation is considered to cause asymptomatic anaemia through chronic blood loss. It was considered an important public health problem in Sri Lanka [13]. A study done in late 1980's in an urban slum community in Galle reported prevalence of worm infestations as high as 95% with prevalence of hook worm infestations of 20% [14]. However, with improved sanitation and personal hygiene, worm infestations have now become rare. Recent data show that the prevalence of worm infestations is low in Gampaha district (1.8%) and that of hook worm is extremely low (0.27%) [15]. Presently, worm infestations are a health problem only in estate communities where prevalence is reported as 29.0% (hook worm 4.7%) [16]. This data suggest that worm infestations have become a less important aetiology for anaemia and is only relevant in the estate sector.

Public health interventions for prevention of anaemia

Currently, three main public health interventions are used in the prevention of anaemia among children in Sri Lanka. They are multiple micronutrient (MMN) supplementation, intermittent iron/folate supplementation and routine anti-helminthic treatment. MMN supplementation schedule is to provide one MMN sachet (which contains 10 mg of elemental iron and vitamins) per day for two consecutive months at 6, 12 and 18 months. Intermittent iron / folate supplementation refers to provision of oral iron and folic acid once-weekly for two, 12-week cycles to school children. Current guideline on deworming of children recommends regular anti-helminthic treatment (mebendazole 500 mg single dose) once or twice a year.

These public health measures, although useful to a limited extent, have not been supported by strong scientific evidence. Provision of MMN and intermittent iron supplementation have shown to improve iron status in children with ID however, universal supplementation with a view of preventing anaemia in children with normal iron stores is questionable. Less than half of children with anaemia are iron deficient and prevalence of IDA in Sri Lanka is only 7.3%. WHO recommends universal iron supplementation in countries where prevalence of anaemia is over 40%, therefore, this strategy in Sri Lanka would lead to unnecessary iron accumulation in many. Iron is not inert and several complications including increased risk of infection (malaria, diarrhoea and acute respiratory infections) are known to occur due to unnecessary supplementation [17]. With new insights into the high prevalence of β- and α- thalassaemia in Sri Lanka, universal iron supplementation can be detrimental rather than beneficial.

Furthermore, addition of MMN sachet to meals would lead to change in taste of food which could lead to food refusal. Impact of this could be huge as the first round of MMN supplementation coincides with start of complementary feeding. This can lead to unforeseen consequences with a programme which aim to prevent micronutrient deficiencies resulting in macronutrient deficiencies and malnutrition. Also, iron tablets given at school could lead to adverse effects which include nausea, abdominal discomfort, anaphylaxis and unintentional overdose that can be life-threatening [18].

Role of regular anthelminthic treatment with a view of preventing anaemia is controversial, too. Prevalence of worm and in particular hook worm infestations is low in Sri Lanka. Therefore, routine anti-helminthic treatment is unnecessary and a waste of precious resources. Also, confusion of pinworm *(Enterobius vermicularis)* which commonly causes *pruritus-ani* with geo-helminths could leads to worm treatment given inappropriately as the treatment regimens are different.

Public health interventions are costly and use public funds. For example, annual expenditure for MMN programme, intermittent iron/folate supplementation and routine anti-helminthic treatment is reported as rupees 125, 70 and 23 million respectively (personal communication). Therefore, it is timely to re-evaluate the usefulness and cost-effectiveness of these interventions.

Another intervention that has been proposed is iron fortification of rice. Although recommended by the World Health Organization, this approach has several limitations. Firstly, universal iron fortification will lead to serious health problems due to iron overload in individuals who already have high iron stores (eg. thalassaemia) [17]. Secondly, fortification could alter the taste of food which might indirectly lead to macronutrient deficiencies. Thirdly, the cost of these programmes are high and should be considered when evaluating cost effectiveness.

Reducing burden due to anaemia – future directions

Public health interventions combating anaemia should aim to reduce prevalence of anaemia whilst minimising risks. As an alternative to a universal supplementation approach, supplementation of target populations identified with high prevalence of IDA and low prevalence of thalassaemia could be safe and effective (Table 1). Alternatively, a micromapping strategy to identify geographical, socio-cultural, economic or ethnic groups with high prevalence of ID within a district could be implemented. It would be cost effective to carryout surveys to identify these groups considering the financial burden of universal supplementation/fortification. Similarly, routine anti-helminthic treatment should be limited to the districts/populations (eg. estate or slums) where the burden of worm infestations is significant. Dietary modifications to improve quality of food, increased consumption of iron rich food (eg. meat, fish, egg york, pulses, green vegetables) and early introduction of iron containing food during weaning are safe, effective and cheaper approaches.

Another important consideration is to improve capacity to identify aetiology of patients with anaemia. Establishing accurate diagnosis will guide appropriate management and minimise unnecessary supplementation at individual level. ID and *β*-thalassaemia trait can be diagnosed by existing laboratory methods however, diagnosis of α-thalassaemia trait is challenging and can only be done by DNA analysis. Given its high prevalence, α-thalassaemia trait should be considered in every patient with unexplained microcytic anaemia and facilities to diagnose α-thalassaemia should be made available in the public sector. Implementing these strategies will assist in gaining a better insight in to and minimizing the burden of childhood anaemia in Sri Lanka.

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