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Anaemia in Sri Lanka: the missing pieces

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Introduction

Anaemia is a major public health problem contributing significantly to maternal and child morbidity and mortality. Globally 25% of the world's population is affected by anaemia, of which half is due to iron deficiency [1]. Any efforts to mitigate this would be justified by the sheer numbers affected and the impact on global health.

Each county is likely to have different causes of anaemia contributing to the disease burden of that community. It would be inappropriate to apply global statistics to any country and more so to decide public health policy without studying local dynamics.

There are many studies conducted in Sri Lanka assessing prevalence of anaemia in the community [2-6]. Most studies are small and regional with only a few covering the whole island. Some researchers have studied prevalence of anaemia without attempting to identify the cause, whilst most have attempted to identify the role of iron deficiency as a cause of anaemia [2,4,6]. Few others have attempted a broader assessment of micro nutrient deficiencies contributing to anaemia [3,5]. Most of these anaemia surveys have an inherent weakness in ignoring the contribution of non-nutritional causes.

The occurrence of β thalassaemia was first reported in Sri Lanka in 1950 and description of haemoglobin variants Hb E, Hb S and Hb D had been reported by mid-1980 [7-10]. Most of these were restricted to case reports or case series and did not attempt to quantify the disease burden of haemoglobinopathies in the community. The public health specialists largely ignored the existence of haemoglobinopathies and these entities were not included in any of the early anaemia surveys.

The first national epidemiological survey of haemoglobinopathies carried out in 1997 identified that the prevalence of β trait was about 2.2% and that of haemoglobin variants Hb E and Hb S was 0.5% or less [11]. This survey highlighted the burden of haemoglobinopathies in the country but was limited by not being comprehensive enough to include prevalence of β thalassaemia in the survey.

Recent studies have begun to address the contribution of haemoglobinopathies in assessing anaemia burden in the community. In a survey

conducted in 2012, in children aged between 6-59 months, iron deficiency anaemia accounted for only 48% of the causes whilst β thalassaemia accounted for 12%. In a further 30% with hypochromic microcytosis the cause remained undetermined [5].

The island-wide Haemoglobinopathy and Iron Deficiency Survey (HIS) was carried out between 2009-2010 in an adolescent population of 7526. This survey reports that iron deficiency (defined as low serum ferritin and raised soluble transferrin receptors (sTFr)) occurred in 34.9% of the population, but iron deficiency anaemia occurred only in 3.9% of them β thalassaemia and deletional forms of α thalassaemia explained anaemia in another 3% of the population and in another 3% anaemia could not be explained by the above two mechanisms [12]. The same study analysing the cause of low red cell indices in 1963 individuals reported that iron deficiency accounted for 37% of cases and α thalassaemia accounted for a further 21%. In 36% of cases the cause could not be attributed to either iron deficiency or haemoglobinopathies [13]. This study highlighted the hitherto unknown contribution of α thalassaemia to low red cell indices and anaemia in Sri Lanka [13].

What disorders might be causing low red cell indices and anaemia that is not due to iron deficiency or α or β thalassaemia, highlighted in the Haemoglobinopathy and Iron Deficiency Survey?

The HIS did not envisage analysing other nutritional anaemias like folate or B12 deficiency. Previous community surveys done in Sri Lanka have identified high prevalence of these micronutrient deficiencies [3,14]. α thalassaemias occurring due to mechanisms other than the two commonest mechanisms of $\alpha^{3.7}$ and $\alpha^{4.2}$ deletions were not studied in the HIS. A novel deletional α^{0} thalassaemia was reported from Sri Lanka previously [15]. There are over 70 types non-deletional α thalassaemia identified worldwide and it would not be surprising if a few of these were identified in Sri Lanka.

The bigger concern is the lack of systematic studies of other red cell disorders in Sri Lanka. Community prevalence of membranopathies and enzymopathies in Sri Lanka are not known. In India, studies suggest that G6PD deficiency occurs at a rate varying from 2% to 13% in different states [16]. Studies of other enzymopathies and membranopathies have been carried out at expert centres [17]. Research in this field in Sri Lanka is very limited. In 1968 a study of patients admitted to Kegalle Hospital using the screening technique of methaemoglobin reductase (Brewers test) postulated the presence of G6PD deficiency in 1.26% of males and 1.28% of females [18]. The results are surprising given the fact that G6PD deficiency is an X-linked recessive disorder and the study identified a higher prevalence in females. It may be that co-existing oxidative unstable haemoglobins like Hb E would have resulted in false positive results. In a more recent study from hospital attendees from Anuradhapura and Kurunegala, 14% of female and 8% of males, were found to be G6PD deficient [19]. The technique used for the analysis of G6PD enzyme deficiency was a WST-8/1-methoxy PMS method. This technique, unlike the Brewers test, is not affected by haemoglobinopathies. Surprisingly here too more females were affected than males.

The above-mentioned studies did not attempt to assess the degree of anaemia in the patient cohorts and thus it is difficult to make a judgment on the contribution of G6PD deficiency to anaemia burden in Sri Lanka. Quite distressingly, even 50 years after the first studies of enzymopathies there are no established centres, which have the capability to study the full spectrum of membrane disorders and enzymopathies in Sri Lanka. This is in a backdrop where most developed research centres analyse these haemolytic anaemias using next generation sequencing [20].

Developing research capabilities will be essential if we are to understand the true burden and the causes of anaemia in the community. It is imperative that policy makers understand the complexity of the causation of anaemia in the community and the technical and design limitations of available research studies, to prevent implementing misguided policy decisions.

Conflicts of interest

Authors declare that they have no conflicts of interest.

References

1. de Benoist B, McLean E, Egli I, Cogswell M. Worldwide prevalence of anaemia 1993-2005. *WHO Global Database on Anaemia, World Health Organization.* 2008.
2. Atukorala TM, de Silva LD. Iron status of adolescent females in three schools in an urban area of Sri Lanka. *J Trop Pediatr* 1990; **36**(6): 316-21.
3. Hettiarachchi M, Liyanage C, Wickremasinghe R, Hilmers DC, Abrahams SA. Prevalence and severity of micronutrient deficiency: a cross-sectional study among adolescents in Sri Lanka. *Asia Pac J Clin Nutr* 2006; **15**(1): 56-63.
4. Department of Census and Statistics, Health Sector Development Project, Ministry of Health Care and Nutrition, Sri Lanka. *Prevalence of anaemia among children and women in Sri Lanka 2006/2007*. Demographic and Health Survey 2006/2007.
5. Jayatissa R, Gunathilaka, MM, Herath P, Fernando DN. *Iron, zinc and calcium deficiency among children aged 6-59 months.* National nutrition and micronutrient survey. Part II. 2015.
6. Senadheera D, Goonewardene M, Mampitiya I. Anaemia and iron deficiency in pregnant women attending an antenatal clinic in a Teaching Hospital in Southern Sri Lanka. *Ceylon Med J* 2017; **62**(3): 175-83.

7. de Silva CC, Weeratunga CES. Cooley's Anaemia in Sinhalese Children. *Arch Dis Child* 1951: **26**(127): 224-30.
8. Graff JAE, Ikin EW, Lehmann H, Mourant AE, Parkin DM, Wickremasinghe, RL. Haemoglobin E and Blood Groups in the Veddas. *J Physiol* 1954; **127**: 41.
9. Nagaratnam N, Wickremasinghe RL, Jayawickreme, US, Maheson VS. Haemoglobin E syndrome in Ceylonese family. *Br Med J* 1958; **1**(5075): 866-8.
10. Nagarathnum NA. Survey of sickling and hemoglobin D in the southern province of Sri Lanka. *Journal of Ceylon College of Physicians* 1984; **17**: 59-62.
11. de Silva S, Fisher CA, Premawardhena A, *et al*. Thalassaemia in Sri Lanka: implications for the future health burden of Asian populations. Sri Lanka Thalassaemia Study Group. *Lancet* 2000; **355**(9206): 786-91.
12. Allen A, Allen S, Rodrigo R, *et al*. Iron status and anaemia in Sri Lankan secondary school children: A cross-sectional survey. *PLoS ONE* **12**(11): e0188110.
13. Rodrigo R, Allen A, Manampreri A, *et al*. Haemoglobin variants, iron status and anaemia in Sri Lankan adolescents with low red cell indices: A cross sectional survey. *Blood Cells Mol Dis* 2018; **71**: 11-15.
14. Thoradeniya T, Wickremasinghe R, Ramanayake R, Atukorala S. Low folic acid status and its association with anaemia in urban adolescent girls and women of childbearing age in Sri Lanka. *Br J Nutr* 2006; **95**(3): 511-6.
15. Suresh S, Fisher C, Ayyub H, *et al*. Alpha thalassaemia and extended alpha globin genes in Sri Lanka. *Blood Cells Mol Dis* 2013; **50**(2): 93-8.
16. Mukherjee MB, Colah RB, Martin S, Ghosh K. Glucose-6-phosphate dehydrogenase (G6PD) deficiency among tribal populations of India – Country scenario. *Indian J Med Res* 2015; **141**(5): 516-20.
17. Warang P, Kedar P, Ghosh K, Colah R. Molecular and clinical heterogeneity in pyruvate kinase deficiency in India. *Blood Cells Mol Dis* 2013; **51**(3): 133-7.
18. Nagaratnam N, Leelawathie PK, Weerasinghe WMT. Enzyme glucose-6-phosphate dehydrogenase (G6PD) deficiency among Sinhalese in Ceylon as revealed by the methaemoglobin reduction test. *Indian J Med Res* 1969; **57**(3): 569-72.
19. Gunawardena S, Kapilananda GMG, Samarakoon D, *et al*. Prevalence of G6PD deficiency in selected populations from two previously high malaria endemic areas of Sri Lanka *PLoS One* 2017; **12**(2): e0171208.
20. Kim Y, Park J, Kim M. Diagnostic approaches for inherited hemolytic anaemia in the genetic era. *Blood Res* 2017; **5**2(2): 84-94.

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