

STOP THE PRESSES

Research Priorities in the field of Anaemia in India

Anju Sinha¹, Bharati Kulkarni², Prasanna Mithra³, Preetam Mahajan⁴, Ravi Upadhyay⁵, Sree kumar Nair⁶, R.S. Sharma⁷

¹Indian Council of Medical Research, New Delhi; ²National Institute of Nutrition, Hyderabad; ³Public Health Evidence South Asia (Manipal University), ⁴AIIMS Bhubaneswar, ⁵Society for Applied studies, New Delhi, ⁶Public Health Evidence South Asia (Manipal University), ⁷Indian Council of Medical Research, New Delhi

| | | | | | | | |
|--------------------------|------------------------------|-----------------------------|-------------------------|----------------------------|----------------------------|--------------------------|----------------------------------|
| Abstract | Introduction | Methodology | Results | Conclusion | References | Citation | Tables / Figures |
|--------------------------|------------------------------|-----------------------------|-------------------------|----------------------------|----------------------------|--------------------------|----------------------------------|

Corresponding Author

Address for Correspondence: Dr Anju Sinha, Indian Council of Medical Research, New Delhi

E Mail ID: apradhandr@gmail.com



Citation

Sinha A, Kulkarni B, Mithra P, Mahajan P, Upadhyay R, Nair SK, Sharma RS. Indian J Comm Health. 2018; 30, Supp: 115-118.

Source of Funding: Nil **Conflict of Interest:** None declared

This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).

Background

Anaemia is a health problem that caused most disability in India over a decade (2005-2016) according to the Global Burden of Disease study(1). India has the maximum number of anaemic women and children in the world(2). As per the recent National Family Health Survey-4 (2015-16), about 58% children (6-59 months), 53% women (15-49 y) and 23% men were suffering from various degrees of anaemia(3). Anaemia affects the general health of the total population taking toll for high mortality as well as morbidity and attenuating the optimal expression of the potentials of both physical and mental capacity of our population. Improving nutritional status of the vulnerable sections of the population and reducing anaemia is of paramount importance for improving health and the human capital development in the country(4).

Prophylactic iron folate supplementation to vulnerable groups has been a part of Government of India program for over three decades. Use of iron supplementation to address anaemia addresses 50-60% of the problem. However, the prophylactic approach may be inadequate to address moderate and severe anaemia cases in absence of universal screening and treatment with therapeutic doses. There are logistic supply chain issues and widely recognized problems with compliance. Anaemia

therefore remains a high priority topic for research as despite the efforts of the government, it is still a very challenging public health problem.

NFHS-4 data show that the levels of IFA (Iron folic acid) intake remain low. For example, only about 30 % of women reported consuming IFA tablets for 100 days or more when they were pregnant(5). There are significant challenges in reaching the at-risk population as well as improving compliance. The country has a prevention and treatment program that is universal in intent. However the extent to which it reaches the masses varies by the ease of access and feasibility of contact.

It is clear that the current rate of decline in the prevalence of anaemia is insufficient to meet the Global Nutrition Target 2025 and the situation prompts us to re-examine the current approaches for control of nutritional anaemia in the country.

Under this premise, the ICMR set up a task force on childhood and adolescent anaemia, to brainstorm, evaluate the evidence and prioritise research questions for immediate implementation, under the chairmanship of Prof. M.K. Bhan.

The coordination unit, ICMR commissioned an overview of reviews based on Cochrane and non-Cochrane systematic reviews, aiming to contextualize the evidence on Anaemia. Additionally, a trend analysis of existing data from

the national surveys was conducted and a document based on recent conferences was prepared and shared with the task force committee. These efforts were geared towards out of the box thinking to result in most appropriate research questions, to be taken up in research mode immediately.

The deliberations by the task force committee and presentations by subject experts would lead to proposal development and study implementation. In the past good research has been helpful for the national programs on Diarrhoea, Pneumonia, Tuberculosis & Immunization. Evidence based interventions helped in achieving a 75% decline in diarrhoeal deaths in 1980s(6). A continuous web of mission mode quality research projects needs to be created around the national programs. However, implementation of quality research depends on a very strong managerial team and resources such as laboratory facilities, expertise in field work, and food technology along with an efficient team of leading researchers. A larger pool of money should also be made available for research. Decisions by expert committees cannot be creative as they focus on consensus rather than on evidence. The present task force committee on childhood and adolescent anaemia was unique in the sense it put the current best evidence at the forefront to formulate its recommendation.

The interventions for control and prevention of childhood and adolescent anaemia: an overview of systematic reviews(7). The overview included Cochrane reviews as well as systematic reviews outside the Cochrane. The search yielded 2601 records, after screening of titles and abstracts, 2040 records were excluded and duplicates were removed. 161 full text articles were assessed for eligibility, 115 were excluded with reasons. Finally 46 systematic reviews were included in the overview, 19 evaluating the effects of iron supplementation, 9 evaluating effects of food fortification, 8 included both supplementation and fortification, 4 evaluated effects of food diversification and 3 evaluated deworming, one each evaluated the effects of treatment for H. Pylori, WASH intervention and anti Malaria treatment. 14 out of 19 systematic reviews reported improvement in anaemia with iron supplementation. However with fortification, most of the SRs reported mixed results. Uniformly, multi-nutrient interventions had better outcomes related to anaemia and home fortification with MNP was

reported to improve the anaemia status among children. For the WASH interventions - available evidence is suggestive of a benefit for growth in children under five years of age and not anaemia.

The recent national surveys and various data sources related to anaemia were analysed to study and map out the trends in anaemia among children, women, and men across various states in the country. It was highlighted that data sources like Annual Health Survey, District Level Health Survey, and National Family Health Survey weren't directly comparable due to procedural differences. An innovative idea describing a prescriptive approach for the required average anaemia reduction rates (AARR) was discussed. Each Indian state would require a different AARR to achieve the anaemia reduction targets for the year 2025 for under five children and women in reproductive age. There is a need to focus on diagnosis and treatment besides supplementation to reduce the prevalence of anaemia in India and achieve the required AARR. There would be a need for monitoring and evaluation indicator framework. A novel concept of anaemia control index for measuring performance of various states was shared with the task force committee (being published elsewhere).

Coexistence of a preventive supplementation (building iron stores) and fortification strategy is considered beneficial. However, in absence of universal screening, adding fortification to the ongoing supplementation program may add a risk of over dosage, especially for iron replete population. However, in view of poor coverage of the current supplementation program, the strategy to use both approaches might be safe during the next decade.

During the meetings the experts working in the area of anaemia presented their research ideas through brief presentations. A discussion was held on the research questions proposed. In this process a blueprint for future research on anaemia has been laid out for uptake. A list of research questions based on the presentations and discussions that followed is given below.

List of research questions

Implementation Research: In order to accelerate the rate of decline in prevalence of anaemia in different states of India and in order to address unmet gaps for different context and setting implementation research should be attempted. Studies on etiology of anaemia, tools for its measurements and the

potential interventions for alleviation of anaemia need to be reviewed. It was suggested to test the feasibility of delivering weekly or biweekly dose iron by ASHA as proposed in the current NIPI program.

Research in the area of technology innovation: for measuring compliance to iron supplementation (urine, breath based test) should be promoted.

Point of Care Diagnostics: comparison of invasive and non-invasive point of care devices against a gold standard and also POC to help devise an algorithmic approach (RBC indices) for Hemoglobinopathies was suggested.

Research on secondary data: Secondary data analysis (from different sources, annual health survey, NFHS, National sample survey) should be attempted to study relationship between reported coverage and decline in anaemia. Secondary analyses to find the determinants of anaemia using spatial data analysis should also be initiated.

Dose of iron related: Considering the current dosage in the program as high, is there a need to decrease the dose? What is the advantage of using 100 mg instead of 60mg iron? Whether lowering of dose would have consequences on compliance and side effects? What is the optimum dose for treatment response, tests to be done in absence of optimum response. Dosing studies should be conducted and dose response, side effects should be better understood.

Anaemia of Pregnancy: Evaluate treatment approach and measure non response by cause in all age groups. Screen, test and treat approach at population level, vs the current program to determine optimal dosing regimens for management of anaemia in pregnancy including injectables.

Childhood Anaemia: The child survival project has achieved a lot and now is the time to act on the thrive agenda for ages up to 2 years. Early onset of anaemia in this age group probably due to delayed or faulty weaning practices need to be studied. Home care program for children 4-18 months through ASHA worker was proposed. Interventions for complimentary feeding, Fe, Vit A, hand washing were suggested.

Adolescent Anaemia: The Weekly Iron & Folic acid Supplementation (WIFS) program is ongoing in many

states. An impact evaluation of WIFS program by a third party was suggested.

Fortification: Efficacy of Point of use Multiple Micronutrient Powder (MMP) Vs. Double Fortified Salt. What is the best combination of micronutrients in a MMP. If multiple foods prepared for ICDS are all fortified what is the cumulative benefit. Calculation of item wise cost and total iron delivered need to be initiated.

Novel Iron delivery methods: Use of nanotechnology for oil fortification with micronutrients is being piloted. If successful a larger study should be planned to test feasibility and efficacy.

Research addressing Biology: Hepcidin as a predictor of response to oral iron should be studied.

Etiology of anaemia: what are causes other than iron deficiency & Bioavailability of iron from enteric coated tablets are long standing unanswered research questions.

The Task Force initiative:

The current rate of decline in prevalence of anaemia is insufficient to meet the global Nutrition Target 2025. Currently under the National Iron Plus Initiative (NIPI) program a life cycle approach has been proposed. The program is being rolled out in the states; however, several gaps due to logistic supply chain, compliance and poor coverage remain. The etiology of anaemia is not considered within this universal approach with IFA. Differentiation based on presence of anaemia and its severity (mild moderate & severe) is not done. Based on this premise the committee recommended a public health approach to anaemia by building up a screen, test and treat approach at population level, vs the current program. The proposed interventional trial would assess the role of a 'Screen test and treat' approach for anaemia at the community level (through a Cluster RCT) and compare it with the current national program focussed on prevention of anaemia through universal prophylactic doses only. This approach may be inadequate to address moderate and severe anaemia cases in absence of therapeutic doses. The research question being addressed is: Does screening for presence of anaemia, testing for its cause and instituting appropriate treatment would lead to a greater

decline in prevalence of anaemia as compared to the present rate of decline in the national program.

Anaemia in children (4-24 months) has negative consequences on cognitive development, school performance, physical growth and work productivity later in life(8). The current National Iron Plus Initiative advocates biweekly IFA supplementation (20 mg of elemental iron and 100 mcg of folic acid) to all children aged 6 to 59 months(9) Low compliance with IFA supplementation has been suggested as an important reason for the lack of adequate success in reducing the high burden of anaemia. However, we need to determine whether this is really so. Are there additional unexplored causes that could account for the slow decline in anaemia prevalence? Can we accelerate the rate of decline?

Deficiency of other micronutrients may have a role in sub-optimal reduction in anaemia, increase in haemoglobin levels when solely focussing on iron supplementation alone(9) Micronutrients helpful in erythropoiesis such as zinc, copper, vitamin B12, B6, A, C, E and D, folic acid and riboflavin improve iron status and up-regulate erythropoiesis through different mechanisms. The second trial (RCT) would assess the benefit of supplementation with multiple micronutrients proven effective in erythropoiesis, in addition to iron and folic acid alone. The task force committee recommended examining whether providing erythropoiesis-relevant micronutrients, in addition to IFA alone leads to a greater increase in hemoglobin concentration and subsequent reduction in anaemia prevalence, compared to supplementation with IFA alone.

ICMR Task Force will steer the implementation of these task force studies, that have the potential to modify the way current national program is being delivered. Preparations for these two ICMR task force studies are underway.

Acknowledgement

We acknowledge all members of the ICMR Task Force on Childhood and Adolescent anaemia for their valuable contributions: Dr. M.K.Bhan, Ex Secretary Dept. of Biotechnology, GOI (Chairman), Dr. HPS Sachdev, SBISR, New Delhi, Dr. Prema Ramachandra, NFI, New Delhi, Dr. Umesh Kapil, AIIMS, New Delhi*, Dr. Anura Kurpad, St. John's Research Institute, Bangalore*, Dr. Molly Jacob,

CMC, Vellore, Dr. Sila Deb, MoHFW, New Delhi, Dr. L Jayaseelan, CMC, Vellore, Dr. Madhvan Nair, Former Scientist 'G', NIN, Hyderabad, Dr. Nita Bhandari, SAS, New Delhi*, Dr. Ranadip Chowdhury, SAS, New Delhi, Dr. Sunita Taneja, SAS, New Delhi, Dr P. Raghu, Sc 'E', NIN, Hyderabad, Dr. Balakrishna, Sc 'E', NIN, Hyderabad, Dr. Meshram, Sc 'E', NIN, Hyderabad, Dr. G.S Toteja, Sc G & Head, Div. of Nutrition*, Dr. Reeta Rasaily, Sc. 'F', CH, Dr. Ajit Mukherjee, Sc. 'F', NIMS,

References

1. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*. 14 Sept 2017; 390; 1211–59.
2. 2017 Global Nutrition Report. <http://www.who.int/nutrition/globalnutritionreport/en/>. Accessed 11.4 2018
3. Ministry of Health and Family Welfare, G.o.I., National Family Health Survey (NFHS-4), State Fact Sheet. Mumbai: International Institute for Population Sciences; 2015–16.
4. Benoist, B.d., et al., Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia. Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia., 2008.
5. WHO. Global nutrition targets 2025: anaemia policy brief (WHO/NMH/NHD/14.4). Geneva: World Health Organization; 2014.
6. Victora CG, Olinto MT, Barros FC, Nobre LC. Falling diarrhoea mortality in Northeastern Brazil: did ORT play a role? *Health Policy Plan*. 1996Jun;11(2):132-41. PubMed PMID: 10158455.
7. Prasanna Mithra, Anju Sinha, Nithin Kumar, Ramesh Holla, Bhaskaran Unnikrishnan, MahalaquaNazliKhatib,RatheebhaiVijayamma, N Sreekmaran Nair. Interventions for the control and prevention of anaemia among children and adolescents: an overview of systematic reviews. PROSPERO 2016:CRD42016053687 Available from http://www.crd.york.ac.uk/PROSPERO_REBRANDING/display_record.asp?ID=CRD42016053687
8. WHO/UNICEF/UNU. Iron deficiency anaemia: assessment, prevention, and control. A guide for programme managers. Geneva: World Health Organization 2001. Available at: http://apps.who.int/iris/bitstream/10665/66914/1/WHO_NHD_01.3.pdf?ua=1, Accessed on 05.03.2018
9. Guidelines for control of iron deficiency anaemia. National Iron Plus Initiative. Ministry of Health and Family Welfare. Available at http://www.pbnrhnm.org/docs/iron_plus_guidelines.pdf, Accessed on 05.03.2018