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COMMENT

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Exploring a spatial template for targetted supplementation of vitamin A in under-5 Indian children

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Pediatric Research (2023) 93:1460–1462; https://doi.org/10.1038/s41390-022-02327-x

The World Health Organization (WHO) advocates the practice of universal vitamin A supplementation (VAS) among under-5 children in countries where vitamin A deficiency (VAD) is a serious public health problem (defined as night blindness prevalence ≥1% among children aged 24–59 months, or low serum retinol prevalence ≥20% in children aged 6–59 months).[1] Under this strategy, high doses of prophylactic vitamin A are periodically provided to all eligible children (total nine doses with a gap of 6 months between two consecutive doses) to address VAD and the consequent risks to child health.[1] Due to high burden of childhood VAD in the past, India has been historically regarded as a 'priority' nation for implementation of universal VAS. In alignment with WHO recommendation, there are standing guidelines from the Government of India for providing VAS in all under-5 Indian children (with the first dose usually provided at 9 months of age, i.e. at the time of measles vaccination).[2] However, a considerable decline in the burden of VAD and the attendant health risks in India over the years have led to rising scepticism about whether continuation of the universal VAS programme is justified.[3,4] For instance, the national prevalence of VAD (defined as serum retinol concentrations <20 µg/dL, adjusted for inflammation) among children younger than 5 years was recently estimated to be 15.7% with significant interstate differences,[3] thereby raising questions on the relevance and validity of universal VAS in contemporary India.[3,5] There are also apprehensions that this dated practice of administering massive vitamin A doses indiscriminately to all children in the eligible age range may now do 'more harm than good' by increasing the risk of hypervitaminosis A, especially with the concurrent spurt in vitamin A-fortified common food items (e.g. edible oil and milk).[3,4] Such concerns have also been voiced in other nations.[6] Further, the benefits of universal VAS on child health and survival have supposedly diminished over the years and are no longer applicable, thereby calling for a policy realignment in favour of targetted VAS.[3,4,7]

With this background, the study by Rai that was published recently in *Pediatric Research* is a very timely effort.[8] In that study, Rai aimed to estimate the effect of VAS (as an explanatory variable) on two important outcomes of childhood undernutrition in India, namely, anaemia and anthropometric failure (including wasting, stunting, and underweight). For that purpose, nationally representative cross-sectional data collected in 2015–2016 during the fourth round of National Family Health Survey (NFHS-4) was adapted to a quasi-experimental fixed-effects study design framework, wherein household- as well as mother-fixed effects of VAS on the stated undernutrition indicators were evaluated. Findings from both the models (i.e. household- and mother-fixed effects approaches) showed that VAS had no effect on childhood anaemia or anthropometric failure in India. Consequently, it was inferred that universal VAS may not be effective for mitigating childhood diseases and nutritional problems of interest in India and that targetted VAS may be a more appropriate solution instead.[8]

The NFHS-4 had estimated the prevalence of anaemia and anthropometric failure (viz. wasting, stunting, underweight) among under-5 Indian children in 640 districts encompassing all the states and union territories during the 2015–2016 reporting period (http://rchiips.org/nfhs/districtfactsheet_NFHS-4.shtml). From these district-wise estimates, it is evident that burden of these childhood undernutrition indicators is geographically quite heterogeneous across the country. As reported earlier, this heterogeneity in prevalence was not random but conformed to spatially significant patterns.[9] The districts exhibited positive spatial autocorrelation and further segregated into distinct clusters of 'high' and 'low' prevalence when subjected to local indicator of spatial association (LISA) analysis.[9] Interestingly, our recent work based on the same NFHS-4 data set revealed that VAS coverage among under-5 children in India was not uniform either.[10] There were prominent spatial patterns underlying the distribution of VAS, with LISA analysis unravelling 'hotspots' and 'coldspots' of coverage across the country at the district-level aggregation.[10] Because of these antecedents, it is of interest to investigate the possibility that the distribution of VAS and indicators of childhood undernutrition in India (like anaemia and anthropometric failure) may be spatially related. If the practice of VAS is indeed effective, it would entail a low burden of these undernutrition indicators in areas with high coverage of VAS, and vice versa.

We probed for such spatial relationships (if any) by computing both global and local indicators of spatial association in the bivariate mode (using GeoDa v.1.18.0 platform). Contiguity-based spatial weights were constructed using queen's criteria of first order. Subsequently, prevalence of the childhood undernutrition outcomes of interest (namely, anaemia, wasting, stunting, underweight) in the districts were assessed in relation to their spatially lagged VAS coverage values (i.e. the explanatory variable). We

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Received: 25 August 2022 Accepted: 13 September 2022
Published online: 30 September 2022

Table 1. Global bivariate relationship of vitamin A supplementation (VAS) coverage with the prevalence of various undernutrition indicators among under-5 children across 640 districts in India during the 2015–2016 reporting period.

Undernutrition indicators	Bivariate global Moran's *I*[a]	*z*-value	Pseudo *P* value[b]
Anaemia	0.031	1.694	0.049
Stunting	−0.253	−12.692	0.001
Underweight	−0.044	−2.446	0.008
Wasting	0.151	8.042	0.001

[a]The bivariate global Moran's *I* statistic is a measure of the overall strength of spatial autocorrelation between the explanatory variable (i.e. VAS coverage) and the outcome variables of interest (i.e. prevalence of undernutrition indicators), with possible values ranging from −1 to +1. A positive value indicates an overall positive spatial autocorrelation and a negative value indicates an overall negative spatial autocorrelation between the two variables, without taking into account any inherent correlation between them.

[b]The statistical significance of the Moran's *I* statistic was assessed by a permutation method. It involved constructing 999 permutations computationally to generate a reference distribution of the statistic, that yielded *z* value for the distribution and an accompanying pseudo *P* value. A pseudo *P* value >0.05 favours the null hypothesis signifying spatial randomness (i.e. overall absence of any spatial pattern), whereas value <0.05 rejects the null and supports the alternate hypothesis (i.e. the presence of an underlying spatial pattern).

specified a default alpha threshold of 0.05 for detecting statistical significance. The global analysis reflected the overall spatial pattern. It indicated that VAS coverage and certain undernutrition outcomes were spatially associated (Table 1). On the other hand, results from local analysis delineated the locations where the spatial relationships were statistically significant. The default findings were followed up by sensitivity analysis using a more stringent alpha cut-off at 0.01. Four different types of significant spatial patterns were observed (viz. high–high, low–low, high–low, and low–high), which were captured through the bivariate LISA maps (Supplemental Fig. 1). Of these, the high–high and low–low regions indicate clustering of similar values (spatial clusters). Specifically, high–high (dark red colour) regions represented locations where prevalence of the undernutrition indicators was high and value of the explanatory variable (i.e. VAS coverage) in the surrounding was also high; and low–low (dark blue colour) regions were those where both the values were low. On the contrary, the high–low and low–high regions indicate spatial outliers. The high–low (light red colour) regions were essentially those locations that witnessed high prevalence of the undernutrition indicators with low coverage of VAS in the surrounding, while the low–high (light blue colour) regions were locations that displayed the opposite scenario. The findings suggest that relationship between the spatial distribution of VAS and the concerned childhood undernutrition indicators was different in different parts of the country. From the programme point of view, it is plausible that the high–low spatial outliers were those regions with low coverage of VAS where the scaling up of vitamin A delivery may be useful in mitigating the high undernutrition burden. Similarly, the low–high spatial outliers were regions where high coverage rates of VAS had apparently helped in reducing the prevalence of undernutrition indicators. Conversely, the high–high and low–low spatial clusters were areas where the VAS programme had possibly no influence on the prevalence of the examined undernutrition outcomes.

While these are interesting propositions that arise from the observed spatial associations and patterns, the plausible causal relationships and effectiveness of VAS (or the lack of it) in the different spatial locations (outliers/clusters) need to be substantiated. For example, it is desirable to know whether the high undernutrition prevalence in the high–low regions is actually attributable to the low VAS coverage rates, and so on. However, well-meaning formal experimental studies (such as placebo-controlled trials) for decisively establishing these associations may not be presently feasible due to ethical concerns, especially in people with documented VAD. In that context, it may be worth extending Rai's quasi-experimental work based on NFHS-4 secondary data[8] and perform subgroup analysis separately by each of the four location types (high–high, low–low, high–low, and low–high). It would help in detecting whether there are indeed differential effects of VAS on childhood undernutrition outcomes in the country across the four locational subgroups. Amidst growing calls for alternatives to universal VAS,[3,4,7,8] more so in a vast and diverse developing nation like India, granular insights into such spatially relevant relationships may help in developing an informed template for planning targetted and customized VAS delivery. In fact, it would be even more insightful and actionable to ascertain whether the coverage of VAS and the prevalence of VAD across the country are spatially related, which is currently precluded by the unavailability of reliable district-level estimates of the latter.

DATA AVAILABILITY

The National Family Health Survey (NFHS-4) data used in this work are available in the public domain at http://rchiips.org/nfhs/districtfactsheet_NFHS-4.shtml. Besides, the literature that forms the basis of this commentary are provided in the list of references. No other data sources were utilized in this work.

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AUTHOR CONTRIBUTIONS

K.B. conceived the manuscript, analysed the data and drafted the paper. T.B. contributed to data management and analysis. Both authors revised the manuscript critically for intellectual content and approved the final version.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41390-022-02327-x.

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