Does cereal, protein and micronutrient availability hold the key to the malnutrition conundrum? An exploratory analysis of cereal cultivation and wasting patterns of India [version 2; peer review: 1 approved with reservations, 1 not approved]

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Abstract

Background: High prevalence of maternal malnutrition, low birth-weight and child malnutrition in India contribute substantially to the global malnutrition burden. Rural India has disproportionately higher levels of child malnutrition. Stunting and wasting are the primary determinants of child malnutrition and their district-level distribution shows clustering in different geographies and regions.

Methods: The last round of National Family Health Survey (NFHS4) has disaggregated data by district, enabling a more nuanced understanding of the prevalence of markers of malnutrition. We used data from NFHS4 and agricultural statistics datasets to analyse relationship of area under cereal cultivation with the prevalence of malnutrition at the district level. We analysed malnutrition through data on under-5 stunting and wasting; maternal malnutrition was assessed through prevalence of women's low BMI and short stature by district.

Results: Stunting and wasting patterns across districts show a distinct geographical and age distribution; districts with higher wasting showed relatively high prevalence of 40% before six months of age. Wasting was associated with higher cultivation of millets, with a stronger association seen for jowar and other millets (Kodo millet, little millet, proso millet, barnyard millet and foxtail millet). Stunting was associated with cultivation of all crops except other millets. Low
women's BMI was seen associated with cultivation of rice and millets. The analysis was limited by lack of fine-scale data on prevalence of low birth-weight and type of cereal consumed.

**Conclusions:** Multi-site observational studies of long-term effects of type of cereals consumed could help explain the ecogeographic distribution of malnutrition in India. Cereals, particularly millets constitute the bulk of protein intake among the poor, especially in rural areas in India where high prevalence of wasting persists.

**Keywords**
Millets, malnutrition, wasting, stunting, MTORC1 (mechanistic target of Rapamycin complex1), GCN2 (general control non derepressible 2), DSCQ (District subsistence cultivation quantum)
Introduction

Globally, the World Health Organization (WHO) estimates that among children under five, about 151 million suffer from stunting and 51 million from wasting with consequent risks of mortality, morbidity and delayed development. The latest stunting trends indicate increases in Africa along with substantial reductions across Asia. However, with regards to wasting, South Asia accounts for half of all wasted children globally.1 Stunting (low height for age), mid-upper-arm circumference (MUAC) less than 125 mm and wasting (low weight for height) are the primary measures of prevalence of under-5 malnutrition.2-3. Children with stunting and wasting both have reduction in muscle mass, albeit greater in the latter, which reduces the pool of available alanine and glutamine for gluconeogenesis, which in turn is essential for supply of glucose to the brain for functioning. Children with wasting also have reduced fat mass, which contributes to a depressed immune response through leptin.4 Children having both stunting and wasting have the greatest risk of mortality. Indeed both are interlinked; wasting earlier in infancy contributes to stunting within a few months to a year.5 Nationwide surveys, in fact, often reveal a mix of both in any population. Further, children with both stunting and wasting are the most vulnerable to mortality due to infections, and hence regions with high prevalence of stunting and wasting are likely to also report higher infant mortality.6,7. India has a disproportionately high prevalence of stunting; there are 62 million stunted children accounting for 40% of the global total, despite having 20% of the world population.8. The socio-economic gains and poverty reduction of the past decades have not translated into commensurate reduction of stunting and wasting in children, often characterised as, the Asian enigma.9-11.

Early onset of malnutrition in India

Historically distinct forms of severe malnutrition referred to as Kwashiorkor and Marasmus are today captured under the umbrella term severe acute malnutrition (SAM). SAM is recognised to have a range of clinical manifestations with a multifactorial causation.12. While some of the risk factors of malnutrition are proximate, related to maternal and household characteristics, distal factors related to the wider socio-economic environment have also been attributed.13-15. Poverty, poor sanitation and hygiene in and around households, are important social determinants that can act across households and geographies causing clustering of malnutrition in entire regions. Ultimately, the proximate causes of morbidity and mortality in severe malnutrition could be recurrent infections probably culminating in environmental enteric dysfunction (EED) with contributions from household nutritional factors (including breast feeding and complementary feeding) and maternal nutritional status (preconceptionally, as well as during pregnancy and breastfeeding).16-18. Pre-conceptional low maternal BMI is an important contributor to intrauterine growth restriction. Maternal short stature, even after adjustment for socio-economic status, is associated with low birth weight, child stunting, delivery complications and increased child mortality.19.

Subsistence farming and millet dependence

Indian states consist of 640 districts (at the time of NFHS4) with wide differences in geography, climate and the main agricultural crops. India has a large and poor rural population (68.9% rural with 25.5% rural poverty prevalence), and over half (54%) of the working rural population (481.9 million) are cultivators and agricultural labourers.20,21. Small land-holding farmers (owning less than two hectares of land) and their families constitute more than half the country’s population. Only half (96.46 million hectares) of the total area under cultivation (198.36 million hectares) is irrigated.22. Although, rice and wheat together constitute 75% of total area under food grain cultivation, Jowar (Sorghum) and Bajra (pearl millet) make up a significant 13.8%. However, the distribution of food grain cultivation in irrigated land varies, with rice (60%) and wheat (94.2%), expectedly being grown largely in irrigated land. In contrast, Sorghum (Jowar) and Pearl millet (Bajra) are grown largely in non-irrigated lands, most likely by small land-holding farmers in monsoon-dependent
arid or semi-arid regions of the country, which are also among the poorest\textsuperscript{3,4}. Household food grain consumption and diets in such regions are likely driven by these strong linkages between agro-climatic and eco-geographic factors, more so among poorer households with socio-economic barriers to achieve dietary diversity.

The latest completed round of National Family Health Survey 4 (NFHS 4) was published in 2015 with district-level data for the first time\textsuperscript{4}. Based on unpublished field observations of wasting prevalence among populations depending on millet as staple in rural Maharashtra (spanning western and central India), we critically examined the spatial patterns of prevalence of stunting and wasting at the district level across India with the objective of exploring the role of dietary staple cereal consumption pattern as a possible explanation. Further, we propose a hypothetical pathway that integrates evidence emerging from agro-climatic and geographic patterns with physiological mechanisms of malnutrition.

**Methods**

We analysed district-level secondary data on under-5 stunting and wasting as well as short stature and low body mass index (BMI) of women of the 15–49 years age group with crop cultivation to assess geo-spatial overlaps and analyse relationships between malnutrition and subsistence cultivation of millets. We included other socio-demographic variables which are known to be associated with malnutrition and assessed their relative contribution to wasting, stunting, short stature and low BMI of women at district level using multivariable linear regression.

**Definitions and data sources**

We considered the following millet crops widely grown and reported in Indian agriculture databases and the Directorate of Millets Development (under Department of Agriculture, Co-operation and Farmers Welfare) in our analysis, henceforth mentioned as millets: jowar (sorghum), bajra (pearl millet) and other millets (Kodo millet, little millet, proso millet, barnyard millet and foxtail millet). The initial hypothesis of the association between children presenting with severe malnutrition and millets was in locations with staple consumption of millets other than ragi (finger millet). Furthermore, Ragi has a relatively better nutritional profile and belongs to a distinct sub-family in the grass family Poacea\textsubscript{e}\textsuperscript{5,6} We did not include Maize in the analysis as, in India, only 20% of maize is consumed, with remaining being utilised for other purposes\textsuperscript{7}.

We adopted the definitions of districts with high prevalence of wasting and stunting from district-level malnutrition analysis by Junaid and Mohanty\textsuperscript{8}, which has considered >45% district-level stunting prevalence, and >27% district-level wasting prevalence as high. We used levels of > 30% and > 15% as high prevalence of women’s BMI (<18.5) and short stature(< 145 cms) respectively.

We extracted variables of interest (district level data on prevalence of stunting and wasting among children under five years of age, utilization of anganwadi, dietary diversity in age 6–23 months, short stature, BMI <18.5, proportion of women with >10 year education, proportion of households in lowest two wealth quintiles and open defecation) from NFHS4. NFHS is a standardised and periodic nationally representative survey. NFHS4 covered 601,509 households, 699,686 women aged 15–49 years and 103,525 men aged 15–54 years that provides comprehensive data on various aspects of maternal and child health\textsuperscript{9,10}. NFHS-4 provides unit level data (for each of the 640 districts of India at the time of survey) for download upon request via the demographic health survey data repository\textsuperscript{10,11}. We extracted data on population of each district from the 2011 Census\textsuperscript{12}.

For data on cultivation of cereal crops, we used DACNET, a web-based land use statistics information system maintained by the Agriculture Informatics Division of the National Informatics Centre of the Government of India\textsuperscript{12}.

From each of the three data sources mentioned above, the following data were extracted to prepare a district-level dataset for analysis\textsuperscript{13}:

1. From the 2011 census data, district-wise total and rural population
2. From the NFHS4 data,
   a. using appropriate weights district-level percentages of BMI of women 15–49 years age group, short stature and women with 10 years or more education from women dataset
   b. district-level percentage of wasting and stunting was calculated from the children dataset
   c. percentage of people in household wealth quintiles, open defecation for a given district was calculated from household dataset
3. Various crop data is available in state-wise reports compiled by the Ministry of Agriculture and Farmers Welfare. We extracted district-level area under cultivation of cereals: rice, wheat, maize, ragi and millets (by type as defined above) into a spreadsheet. Data was from the latest state-wise reports available at the time of analysis at DACNET\textsuperscript{12} (data for most states ranged for years between 2014–17 except Maharashtra 2002–03, Manipur 2004–05 and Gujarat 2007–08; all data in hectares converted to acres).

Using district names as the common variable in all three datasets, they were merged. Any errors due to district spellings and duplicate district names across differing states were handled with caution to ensure proper merging. For each district we estimated the population of poor by multiplying the census figures for population of the district by the proportion of the population in the fourth and fifth wealth quintiles (from NFHS4). This was based on the assumption that subsistence millet consumption...
is largely restricted to poor small land-holding farmers\textsuperscript{14,15}. District Subsistence Cultivation Quantum (DSCQ) for each district was obtained by multiplying the per capita area (cereal cultivation area in acres/total population) by the proportion of the poor (in the lowest two wealth quintiles as per NFHS) followed by normalising data using logarithmic transformation.

Variables

Variables from three data sources (NFHS-4, census 2011 and agriculture cultivation data) were combined into a single dataset\textsuperscript{16}.

Independent variables. We used per capita area under cultivation of crops and the DSCQ for each cereal. Except for areas in economically better-off and well-irrigated regions, particularly in northern India\textsuperscript{14,40}, where bajra and jowar are grown for animal fodder and other purposes; elsewhere, millets are cultivated largely by small land-holding rural poor farmers and for subsistence purposes\textsuperscript{17}. Other socio-demographic variables included in our analysis are prevalence of BMI <18.5 among women in 15–49 years age-group, short stature(<145 cm height) among women in 15–49 age-group utilization of anganwadi, dietary diversity (age 6–23 months), women 10 year or more defecation and rural population.

Outcome variables: percentage of children with wasting (weight for height <-2SD), percentage of children with stunting (height for age <2 SD).

Analysis

Spatial malnutrition patterns. We assessed overlaps between high prevalence of stunting and/or wasting with cereal cultivation data by generating maps derived from The Database of Global Administrative Areas (GADM)\textsuperscript{46}. We merged tabular data (from a spreadsheet file) with geographic data (from a geojson file), chose variables of interest, created map legends dynamically and rendered multiple maps using a custom-built wrapper software written in javascript which internally uses Mapbox GL JS library (version 1.10.0) for rendering maps\textsuperscript{47}. Further information on what this software wrapper does and how it works is present in the README file of the source code\textsuperscript{48}. As a base layer, DSCQ was shaded using a linear interpolator with manually chosen colour levels for the legend. A transparent layer of outcome variables (stunting and wasting, low BMI and short stature) marked with distinct stripe patterns was overlaid on the base layer for visualizing overlap.

Examining relationship between subsistence millet cultivation, childhood malnutrition and its early onset. For each cereal, we examined its association with district-level prevalence of stunting and wasting, as well as the association between maternal factors (women’s BMI and short stature) and DSCQ (normalised using logarithmic transformation) by linear regression. We examined the relationship of age with wasting and stunting at the district level.

Results

Districts with high prevalence of stunting (ranging from 46–65% district prevalence) numbered 108 with higher representation from the poorer states (number of districts followed by percentage given in parenthesis) of Uttar Pradesh (30; 28%) Bihar (28; 26%) and Madhya Pradesh (22; 20%). Districts with higher wasting prevalence (ranging from 28–47% district prevalence) were also 108 in number with predominantly tribal districts of Jharkhand (14; 13%), Madhya Pradesh (19; 18%), Maharashtra (12; 11%), Rajasthan (10; 9%) and Gujarat (10; 9%) having higher representation. High stunting is more concentrated in north and eastern India, whereas high wasting areas are located primarily in central India, along with those districts having both stunting and wasting (Figure 1). There are only 18 districts with both stunting and wasting. Out of them 13 have millets or maize as either the highest (8) or second highest crops (5) (Table 1). Of these 18 districts, there are three from Rajasthan, which have more maize cultivation than any other cereal crop (Udaipur 62%, Banswara 51%, and Dungarpur 47%).

On examining the district-level patterns of subsistence cultivation of millets by district (based on DSCQ of Jowar, Bajra and other millets) overlaid over districts having higher prevalence of stunting and wasting, we find that there is an overlap of districts with wasting alone and those with stunting and wasting with higher DSCQ for millets (Figure 2). However, large areas with higher DSCQ particularly in North, West and some parts of central India do not show either stunting or wasting. Similar maps, separately showing overlap of high stunting and high wasting with per-capita cultivation of jowar, wheat, rice, bajra and other millets are also available\textsuperscript{15}. There is an overlap of districts with high wheat and rice cultivation in the well irrigated Gangetic plain (North and Eastern parts) with stunting. Cultivation of other millets is scattered throughout the country with an overlap with high prevalence of wasting. The large irrigated areas in the Northwest & Central India with high DSCQ of Bajra & Jowar also have higher DSCQ of rice and wheat as seen from the maps (irrigated areas having cultivation of rice, wheat along with Bajra & Jowar). Maize cultivation is all over the country with no clear overlap with either stunting or wasting.

Overall, increase in cultivation of jowar, bajra and other millets is independently associated with increase in prevalence of both stunting and wasting (see Figure 3–Figure 5). When the association was examined for individual millets, whereas jowar cultivation did show an association with increase in both stunting and wasting, increase in bajra cultivation was associated only with increase
in stunting. Increase in cultivation of other millets was associated with increase in wasting only (a reverse trend was seen with stunting). As expected, there was either no change or decrease seen when we examined association between increase in rice or wheat cultivation with wasting (with an increase in stunting associated with increase in rice or wheat cultivation).

On examining the relationship between low BMI and short stature with millet cultivation, we see an association between increase in jowar, bajra and other millets (both when examined individually and altogether) with prevalence of low maternal BMI. For short stature, the relationship with millets was either reversed or there was no relationship (Figure 6–Figure 8).

**Figure 1.** Map of India showing areas with higher prevalence of stunting (>45%) in horizontal bars and those with higher prevalence of wasting (>27%) in vertical bars. Districts with high prevalence of both stunting and wasting are numbered cross-referenced to Table 1.
On examining the high prevalence of low BMI (≥30%; BMI less than 18.5) in women of 15–49 years of age and short stature (≥15% with stature less than 145 cm) in women 15–49 years of age, we found that the areas with higher prevalence of short stature were distributed in the Northern Gangetic plains and Northeast India, whereas the areas with higher prevalence of low BMI were located predominantly in peninsular India. Similar maps, separately showing overlap of high prevalence of low BMI and high prevalence of short stature with per-capita cultivation of jowar, wheat, rice, bajra and other millets are also available. The areas with low BMI overlap over millet-growing areas (Figure 6) in a pattern similar to the prevalence of wasting in children seen earlier (Figure 2).

Table 1. Districts with high prevalence of stunting and high prevalence of wasting as per the integrated dataset from NFHS4 and agriculture statistics.

<table>
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<th>No</th>
<th>District</th>
<th>State</th>
<th>Major crop1</th>
<th>Percentage</th>
<th>Major crop2</th>
<th>Percentage</th>
<th>Major crop3</th>
<th>percentage</th>
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<td>Bajra</td>
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<td>14.87</td>
<td>Maize</td>
<td>12.62</td>
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On examining the high prevalence of low BMI (≥30%; BMI less than 18.5) in women of 15–49 years of age and short stature (≥15% with stature less than 145 cm) in women 15–49 years of age, we found that the areas with higher prevalence of short stature were distributed in the Northern Gangetic plains and Northeast India, whereas the areas with higher prevalence of low BMI were located pre-dominantly in peninsular India. Similar maps, separately showing overlap of high prevalence of low BMI and high prevalence of short stature with per-capita cultivation of jowar, wheat, rice, bajra and other millets are also available. The areas with low BMI overlap over millet-growing areas (Figure 6) in a pattern similar to the prevalence of wasting in children seen earlier (Figure 2).

In districts with high stunting and wasting, wasting showed an early onset with highest wasting (40%) less than 6 months of age (Figure 9). The age-distribution of stunting was similar for both groups of districts (Figure 10). The districts with high prevalence of stunting had highest age-specific stunting prevalence at 12 months with a plateau thereafter till five years of age. The earlier onset of wasting suggests maternal nutritional factors affecting intra-uterine growth during pregnancy and possibly continuing in early infancy while being breast fed.

After accounting for the effects of known co-variates of child malnutrition, cultivation of jowar (β = 0.32, 95% CI: 0.163 - 0.488), other millets (β = 3.372, 95% CI: 1.404 - 5.341), women BMI less than 18.5 (β = 0.211, 95% CI: 0.135 - 0.287) are significant predictors of under-five wasting at district level (Table 2). On the other hand, cultivation of wheat (β = 0.315, 95% CI: 0.191 - 0.439), and women short stature (β = 0.474, 95% CI: 0.376 - 0.571) predict district level stunting (Table 3).
Discussion

Poverty and its antecedents affecting dietary intake, health-care and poor environmental conditions can broadly explain malnutrition prevalence, particularly stunting worldwide. Nearly three decades ago, Victora identified the several-fold variation in wasting prevalence in areas with similar stunting prevalence. Child malnutrition is more common in rural non-pastoral communities pointing to the protective role of milk proteins in

Figure 2. Map of India showing overlap between high prevalence of stunting, high prevalence of wasting with DSCQ of Jowar, Bajra and other millets by district.
the mother-child dyad during the first 1000 days; indeed breastfeeding has been linked with intelligence, educational attainment and income security in adult life. In a prescient paper, Martorell et al. highlighted higher levels of early wasting with similar levels of stunting in India, in comparison to Guatemala. They have linked the higher prevalence of low BMI and maternal anaemia in India, while suggesting that improvements in maternal nutrition through prenatal interventions and during breastfeeding could address this problem of early wasting. Apart from this comparative analysis, the current list of possible explanations for the particular patterns of wasting in India include several macro-level and general determinants of malnutrition such as poor status of women, the thin-fat infant phenotype, chronic dietary insufficiency, poor dietary quality, marked seasonality, and poor levels of sanitation. Our analysis attempts to show that ultimately, disaggregation of the data on type of malnutrition prevalence within India at a finer-scale along with proximate dietary factors probably holds the clues to such differences.

Global patterns of wasting linked to millet subsistence
The explanations for ecogeographic patterns of wasting in India appear to at least partially rest in subsistence cultivation patterns and staple consumption of millets as seen in our results. This pattern can be reproduced globally. Subsistence farming of millets is prevalent in other areas with some of the highest

Figure 3. Plots examining relationship between jowar cultivated with stunting and wasting at district level along with map showing the overlap of jowar cultivated with stunting and wasting. A) Scatterplot of stunting v/s district subsistence cultivation quantum of jowar by poor B) Scatterplot of wasting v/s district subsistence cultivation quantum of jowar by poor C) Geographic distribution of district subsistence cultivation quantum of jowar by poor, stunting > 45 & wasting > 28.
prevalence of wasting worldwide such as Yemen and Sub-Saharan Africa. Similarly, in the low-lying areas of Jizan province of Saudi Arabia (which is adjoining Yemen), pearl millet is cultivated and widely used as a staple; expectedly, wasting prevalence in Jizan is the highest among all provinces in Saudi Arabia. Malnutrition in early infancy has been shown in a recent paper to be highly prevalent in India, Niger, Nigeria, Burkina Faso and Mali. These are in fact the top countries that produce millets for human consumption through subsistence farming. A paper by Grellety and Golden brought out differences in patterns of wasting in countries with some having more proportion of wasting due to MUAC, while others had greater proportion of wasting due to less weight for height or both. On examining FAOSTAT data to explain Grellety and Golden’s assessment of differences in types of acute malnutrition across various countries, we found higher prevalence of wasting by MUAC to be a feature of maize-cultivating countries, while the countries reporting low weight for height are typically cultivating millets. These apparent differences in type of malnutrition linked to millets has also been reproduced in observational studies. In a comparison of Bwamanda district (Democratic Republic of Congo with maize and Cassava staple) and Niakhar region (in Senegal with staple millet consumption), the former had higher proportion of wasting measured by lower MUAC, while the latter had earlier onset of wasting and higher prevalence of low weight for heights. At a global level, the top 50 countries ranked among the hidden hunger scores had either maize or millets/sorghum as staple among the top two cereals (as seen from FAOSTAT data of the top two cereals produced).
Cereal protein quality

Sorghum, millets and maize share a common evolutionary ancestor in the grass family (Family Poaceae, sub-family Panicoideae), and can grow in arid/semi-arid agro-climatic regions where other crops often do not produce optimal yields through their dependence on the C4 carbon fixation pathway of photosynthesis. Millets are also usually not traded in markets but consumed directly by poor subsistence farmers. In rural India, the chief source of proteins are cereals. Further, there is a socio-economic gradient to protein quality; tribal populations and the poor consume lesser lysine-containing proteins primarily through cereals. The diet of rural pregnant and lactating women is particularly inadequate with respect to quality of protein, thereby contributing to early malnutrition. Lysine content of millet (22 mg/g of protein) and sorghum (24 mg/g of protein) is the least among cereals in comparison to rice (35 mg/g of protein) and wheat (27 mg/g of protein). The proportionate amino-acid requirement at infancy is the highest and shows an age-related decline. Extensive dependence on millets and sorghum as a staple among millions of poor rural communities where subsistence farming is the mainstay, in semi-arid and rainfed agricultural landscapes, motivated the FAO to commission a detailed assessment of their dietary protein quality. The report unequivocally highlights the inadequacy of millet and sorghum proteins for infants and young children based on amino acid scores. The other inexpensive and subsistence crop in India is maize with only 20% consumption, which (apart from its association with Kwashiorkor in the initial description by...
Cecily Williams) too has been extensively investigated for its causation of Pellagra\(^ {79-81} \). Similarly, Sorghum has been shown to be associated with Pellagra in Indian studies\(^ {82} \). Protein quality is assessed currently by the Digestible Indispensable amino acid scores (DIAAS) as per guidelines of the FAO. The DIAAS of different cereals is shown in Table 4, drawn from a compendium curated by Hans-Henrik Stein of the University of Illinois, Urbana-Champaign (pers comm).

Sorghum protein is stored in Kafirins and is deficient in amino acids lysine with an excess of leucine\(^ {35,36,47} \). Millets in general have higher tannins\(^ {35,36,47} \); pearl millet has antinutrients like phytic acid, goitrogenic polyphenols, and tannins\(^ {84} \). Despite its better amino-acid profile (among the millets) the digestibility of proteins in Pearl millet (bajra) is probably less than other major grains\(^ {36} \) due to antinutrients\(^ {35,36} \).

**Effect of cooking:** In India, the commonest mode of consumption of millets is by milling followed by removal of bran and making unleavened bread using (typically) dry heat\(^ {85} \). Porridge-like preparations and cooked grains are also common. Sorghum protein becomes much less soluble after cooking\(^ {46} \).
Figure 7. Plots examining relationship between bajra cultivated with low BMI and short stature in women’s (15–49) district level along with the map showing the overlap of bajra cultivated with low BMI and short stature in women’s (15–49) A) Scatterplot of low women’s BMI v/s district subsistence cultivation quantum of bajra by poor B) Scatterplot of women’s short stature v/s district subsistence cultivation quantum of bajra by poor C) Geographic distribution of district subsistence cultivation quantum of bajra by poor low women’s BMI and women’s short stature.

These modes of processing are inferior to processes such as fermentation, germination or in combination which increase the availability of micronutrients, such as iron and zinc\textsuperscript{87,88}. Such cultural and social norms are important determinants of bioavailability of nutrients. For instance, maize is consumed in Latin America after nixtamalization, unlike in India where it is consumed directly, possibly explaining the stunting and wasting in the few districts in India where maize-growing for staple consumption is high\textsuperscript{89}.

Ready to use therapeutic food and aminoacids: The focus on protein quality has important biomedical and policy implications. Recent success with the use of peanut paste with milk based ready-to-use therapeutic food (RUTF) is being supplemented with well-intentioned attempts to use locally available ingredients in community-based malnutrition management approaches\textsuperscript{90}. These soya-maize-sorghum (SMS) formulations have been reported to be inferior in trials, particularly in children less than two years of age \textit{vis-a-vis} peanut-based RUTF\textsuperscript{91,92}. However, when supplemented with free amino acids (free aminoacid soya-maize-sorghum RUTF), it has been shown to be as efficacious as standard peanut milk based RUTF\textsuperscript{6} thereby highlighting amino acids to be the missing link in the millet-based RUTF in the first 1000 days of life.
Micronutrient availability from cereals: However, in a poor family with low dietary diversity on a cereal based diet, in contrast to amino acid availability, the intake of micronutrients, particularly Zinc, could be lesser in the pre-dominantly rice and wheat cultivating areas (Table 5). Zinc levels, however, remains unaffected by maternal status and intake in the breast milk\textsuperscript{15}. However, calcium and possibly, Vitamin D are affected by maternal intake in the breast milk\textsuperscript{15}. Ragi is replete with both Calcium and Vitamin D in comparison to other cereals (Table 5). Hence, the higher prevalence of stunting and short stature in rice- and wheat-growing areas (Figure 2–Figure 8) could be due to micronutrient deficiencies.

Cellular pathways to malnutrition
Over the last three decades, pioneering research on cell growth has helped elucidate the critical role of complex intracellular nutrient-sensing mechanisms and their linkages with upstream and downstream pathways incorporating endocrine inputs for growth, primarily centred on the role of protein
Figure 9. Age profile of stunted and wasted children in 108 high wasting (28–47%) districts.

Figure 10. Age profile of stunted and wasted children in 108 high stunting (45–67%) districts.
Table 2. Multivariable Regression models exploring the association between poor, women =>10 years of education, Proportion of rural, Open defecation, Minimum dietary diversity, Utilization of anganwadi, Women short stature, Women BMI less than 18.5, cultivation of Jowar, Bajra, other millets, rice and ragi and the outcome of interest is under 5 wasting.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Model-1</th>
<th>Model-2</th>
<th>Model-3</th>
<th>Model-4</th>
<th>Model-5</th>
<th>Model-6</th>
<th>Model-7</th>
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*** p<0.001, ** p<0.01, * p<0.05
Table 3. Multivariable Regression models exploring the association between poor, women =>10 years of education, Proportion of rural, Open defecation, Minimum dietary diversity, Utilization of anganwadi, Women short stature, Women BMI less than 18.5, cultivation of Jowar, Bajra, other millets, rice and ragi and the outcome of interest is under 5 stunting.

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<thead>
<tr>
<th>Variables</th>
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<td>-0.137***</td>
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<td>0.132***</td>
<td>0.086***</td>
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<td>0.065***</td>
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<td>-0.336***</td>
<td>-0.149***</td>
<td>-0.082***</td>
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<td>-0.048**</td>
<td>-0.068***</td>
<td>-0.038**</td>
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<td>0.612***</td>
<td>0.474***</td>
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<td>(0.796 - 1.007)</td>
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<td>(0.376 - 0.571)</td>
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<td>(-0.011 - 0.304)</td>
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Table 4. Digestible indispensable amino acid scores (DIAAS) determined for human foods using the pig or rat model (Data from published studies compiled by Hans-Henrik Stein, University of Illinois, Urbana-Champaign).

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<tr>
<th>Cereal grains</th>
<th>Animal model/human</th>
<th>Infants(0-6 months)</th>
<th>Young children (6 months–3 years)</th>
<th>Older children, adolescents and adults</th>
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<tr>
<td>Rice, cooked</td>
<td>Rat</td>
<td>--</td>
<td>60 (lysine)</td>
<td>--</td>
<td>Rutherford et al., 2015</td>
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<tr>
<td>Rice, polished, cooked</td>
<td>Rat</td>
<td>--</td>
<td>37 (lysine)</td>
<td>--</td>
<td>Han et al., 2019</td>
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<td>Rice protein</td>
<td>Pig</td>
<td>48 (lysine)</td>
<td>57 (lysine)</td>
<td>Exp. 620*</td>
<td>Cervantes-Pahm et al., 2014</td>
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<tr>
<td>Wheat flour, atta</td>
<td>Pig</td>
<td>--</td>
<td>--</td>
<td>64 (lysine)</td>
<td>Cervantes-Pahm et al., 2014</td>
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<td>Sorghum, raw</td>
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<td>29 (lysine)</td>
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<td>10 (lysine)</td>
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<td>Millet, proso, cooked</td>
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<td>7 (lysine)</td>
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</tr>
<tr>
<td>Corn, yellow dent, raw</td>
<td>Pig</td>
<td>--</td>
<td>--</td>
<td>48 (lysine)</td>
<td>Cervantes-Pahm et al., 2014</td>
</tr>
<tr>
<td>Wheat, whole, cooked</td>
<td>Rat</td>
<td>--</td>
<td>20 (lysine)</td>
<td>--</td>
<td>Han et al., 2019</td>
</tr>
<tr>
<td>Wheat, raw</td>
<td>Pig</td>
<td>--</td>
<td>--</td>
<td>43 (lysine)</td>
<td>Cervantes-Pahm et al., 2014</td>
</tr>
<tr>
<td>Wheat, raw</td>
<td>Pig</td>
<td>37 (lysine)</td>
<td>45 (lysine)</td>
<td>54 (lysine)</td>
<td>Mathai et al., 2017</td>
</tr>
</tbody>
</table>

* Exp 620 stands for Experiment 620 in the Laboratory of Prof Hans-Henrik Stein, University of Illinois, Urbana-Champaign.

Table 5. Micronutrient table for cereals compiled from Indian Food composition Tables 2017, National Institute of Nutrition, Hyderabad, India.  

<table>
<thead>
<tr>
<th>S.no</th>
<th>Cereal Name</th>
<th>In 100 gm of edible portion</th>
<th>Expressed per 100 gm edible portion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Fe (mg)</td>
<td>Zn (mg)</td>
</tr>
<tr>
<td>1</td>
<td>Bajra (Pennisetum typhoidenum)</td>
<td>6.42 (+/- 1.04)</td>
<td>2.76 (+/- 0.36)</td>
</tr>
<tr>
<td>2</td>
<td>Jowar (Sorghum vulgare)</td>
<td>3.95 (+/- 0.94)</td>
<td>1.96 (+/- 0.31)</td>
</tr>
<tr>
<td>3</td>
<td>Maize, dry (Zea mays)</td>
<td>2.49 (+/- 0.32)</td>
<td>2.27 (+/- 0.23)</td>
</tr>
<tr>
<td>4</td>
<td>Ragi (Eleusine coracana)</td>
<td>4.62 (+/- 0.36)</td>
<td>2.53 (+/- 0.51)</td>
</tr>
<tr>
<td>5</td>
<td>Little millet or Samai (Panicum miliare)</td>
<td>1.26 (+/- 0.44)</td>
<td>1.82 (+/- 0.14)</td>
</tr>
<tr>
<td>6</td>
<td>Foxtail millet (Setaria italica)</td>
<td>2.34 (+/- 0.46)</td>
<td>1.65 (+/- 0.18)</td>
</tr>
<tr>
<td>7</td>
<td>Rice, raw milled (Oryza sativa)</td>
<td>0.65 (+/- 0.11)</td>
<td>1.21 (+/- 0.17)</td>
</tr>
<tr>
<td>8</td>
<td>Wheat flour, atta (Triticum aestivum)</td>
<td>1.77 (+/- 0.38)</td>
<td>0.88 (+/- 0.07)</td>
</tr>
<tr>
<td>9</td>
<td>Barley (Hordeum vulgare)</td>
<td>1.56 (+/- 0.15)</td>
<td>1.5 (+/- 0.27)</td>
</tr>
</tbody>
</table>

# For wheat flour refined
kinases, MTORC 1 and MTORC2\(^{96-101}\). Another protein kinase, GCN2 acts in concert with MTORC1 in sensing amino acid deficiencies\(^99\).

From the results above, clearly, there are distinct geographic patterns of both stunting and wasting as well as low BMI and short stature of women of 15–49 years age group. There is also similarity in patterns of association between low maternal BMI with child wasting and maternal short stature with child stunting. Large-scale subsistence cultivation of millets in dry/semi-arid areas of central India are more likely to be associated with higher wasting. Other factors like quantity of food, intake of proteins through milk and other animal sources during and before the first 1000 days by the mother, the dietary matrix and diversity and presence of infections are also important. However, the ecogeographic patterns of malnutrition can probably be explained to some extent by staple cereal cultivation. Hence, an attempt has been made to build

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**Figure 11.** A schematic figure showing the possible pathways linking staple cereal consumption with child malnutrition with key steps highlighted (with references to evidence from literature).
hypothesized framework explaining the plausible pathways through which staple based cereal based diet could produce wasting (Figure 11)

The millet based diet has a low glycaemic index, putative deficiencies in amino acids and micronutrients with variable digestibility after cooking (Figure 11 pathway 2) due to the presence of a tough cell wall and antinutrients. This leads to a greater lowering of amino acids which in turn leads to a substantial lowering of MTORC1 and rise in GCN2 contributing to wasting (Figure 11 pathway 596–100). The lowering of MTORC1 & GCN2 at the cellular level causes low BMI in women (particularly in growing adolescents) with consequent decreased acquisition of nutrients by placental syncytiotrophoblast94,95,102,103.

This in turn leads to intra-uterine growth restriction and low birth weight. These nutritional effects on the malnourished mother persist during breast feeding15 (Figure 11 pathway 6) leading to early wasting and lower weight for height seen in regions with higher wasting (Figure 11 pathway 9)78,85,104,105. Maize consumption without nixtamalization could lead to lesser unbound niacin (Figure 11 pathway 7)68,89,101,106 and both stunting and wasting with lower MUAC (Figure 11 pathway 11)65,67.

Poverty in highly populous areas growing rice & wheat could be contributory to stunting. Possible greater stress, lower dietary quantity and poor sleep could be contributory (Figure 11 pathway 8)12,10,39,107. Lower lysine, high phytales with lowered micronutrients like zinc and iron in cereal based diet in wheat and rice growing areas with poor dietary diversity could lead to stunting (Figure 11 pathway 8)89,94,95,103,109. Infections in the growing child can decrease stimulation of both MTORC1 and 2 through T cell mediated mechanisms (Figure 11 pathway 3)106. Millets are indeed gluten-free, have high fibre and antioxidant content and have recently seen a spike in use109,111–113. However, their use by pregnant as well as nursing mothers and children in poor communities, with limited dietary diversity, during the first 1000 days could be associated with malnutrition.

Study limitations
An important limitation of our analysis is the limited data on low birth weight and food grain consumption at finer scales, which would have allowed for confirmation of our hypothesis at household level. One of the reasons for this is that the NFHS surveys record cereal consumption without paying attention to type of cereal. Indeed, our analysis shows that this is an important change in NFHS and demographic health surveys worldwide that may be needed to gain better understanding of pathways to malnutrition. The use of cereal cultivation as a proxy for consumption too is a source of noise in our data, as some of the cultivation is likely to be for non-human use (primarily fodder). The data on availability of nutrients from millet consumption, as per current nutritional assays (stable isotope-based), is meagre, to the best of our knowledge. Such data from cereal consumption could help in linking the dietary matrix to effects.

Conclusion
Higher wasting and stunting prevalence among children in India has an ecogeographic pattern with plausible links to subsistence millet consumption with the former. MUAC and type of cereal consumed should be incorporated in the anthropometry measures surveyed in NFHS4 and global demographic and health surveys to enable better assessment of patterns of malnutrition. State of the art research in nutrient sensing should be integrated with agriculture, food science, delivery systems and dietary matrix for translational benefits to accrue to the wider population.

Data availability
Underlying data
Figs hare: Dataset used to assess relationship between millet cultivation and malnutrition patterns in India at district level. https://doi.org/10.6084/m9.figshare.12236789.v243

This project contains the following underlying data:
- malnutrition_dataset_for_publication.xlsx (Dataset used for analysis described in the papert)
- Malnutrition and millets – India – DACNET NFHS 4.docx (Word document explaining how the dataset was prepared)

Extended data
Figs hare: Plots examining relationship between type of millet cultivated with stunting and wasting at district level along with map showing the overlaps for each type of millet with stunting and wasting. https://doi.org/10.6084/m9.figshare.12206135.v451

This project contains the following extended data:
- malnutrition_millet and malnutrition.pdf (PDF file with panel of seven plots and maps, each showing relationship between type of millet cultivated with stunting and wasting at district level and the corresponding map showing the overlaps of each type of millet with stunting and wasting)

Figs hare: Plots examining relationship between low BMI and short stature in women 15–49 with stunting and wasting at district level along with map showing the overlaps for each type of millet with low BMI and short stature in women (15–49). https://doi.org/10.6084/m9.figshare.12206264.v452

This project contains the following extended data:
- malnutrition_bmi_short_status.pdf (PDF file with panel of seven plots and maps, each showing relationship between low BMI and short stature in women 15–49 with stunting and wasting at district level along with maps showing overlaps for each type of millet with low BMI and short stature in women (15–49))

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Software availability
Source code available from: https://gitlab.com/asdofindia/malnutrition-crops-maps

Archived source code at time of publication: http://doi.org/10.5281/zenodo.382872550
Acknowledgements

RKS and BK would like to thank the Pravara Institute of Medical Sciences (PIMS) for encouraging research on child malnutrition, in particular, the Dr Rajendra Vikhe Patil (CEO & Pro-Chancellor), Professor (Col) DY Shrikhande (Head of the department of Pediatrics), Professor Rahul Kunkulol (Director of Research) and Professor KV Somasundaram, Director of the Centre for Social Medicine at PIMS. All authors thank Awdhesh Yadav for help with organisation of the final dataset and statistical analysis, Shivanand Savatagi for help with figures and Mahantesh Kamble for help with references.

References

33. Food and Agriculture Organization: State of the world’s forests. 2005. Reference Source


Open Peer Review

Current Peer Review Status: ? ×

Version 2

Reviewer Report 12 January 2021

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Edward J.M. Joy MD
Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, UK

The authors have made substantial revisions which have largely addressed my earlier comments. I would prefer the authors to expand on the study limitations, which are inherent in a cross-sectional, ecological study design.

The multi-variate analysis is a better approach. It appears that the association between wheat consumption and wasting is similarly strong as for jowar consumption, which I suppose illustrates the potential pitfalls with over-interpreting the findings and implying causality via a specific metabolic pathway driven by (anti-)nutritional factors in millets. It would be consistent with an underlying driver of poverty/wealth which will determine not only access to diverse diets but also other risk factors of undernutrition.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Dietary micronutrient assessment, population micronutrient assessment

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Version 1

Reviewer Report 27 July 2020

https://doi.org/10.21956/wellcomeopenres.17478.r39290
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Suparna Ghosh-Jerath
Indian Institute of Public Health-Delhi, Public Health Foundation of India, Gurgaon, Haryana, India

The manuscript provides insight on impact of production of coarse cereals (selective millets) on the nutritional status of women and children in India.

I have the following concerns with the methodology and conclusions drawn in this manuscript:

1. Title: The title has issues in terms of including food (cereals) and nutrients (proteins and micronutrients) in the same basket, which is not clear.

2. Hypothesis: According to the manuscript, families depending on subsistence farming and growing millets may have higher levels of wasting in under 5 children and malnourishment in women. Assessing causality by relating production of millets to nutritional status without looking at actual consumption and other factors [underlying and basic factors (ref to UNICEF conceptual framework of Causes of maternal and child malnutrition)] may be flawed.

3. The issue of assuming causality from correlations with perhaps erroneous conclusions is a major concern in this manuscript. It is crucial to look at dietary consumption data, from NSSO and NNMB and it is also important to adjust for all the other factors like SES, endemicty to diseases, access to potable water before superimposing millet cultivation and prevalence of malnutrition in women and wasting in children. These communities are poverty stricken and have limited access to several resources mentioned above. So the yield of crop is questionable as well. What % of their farming are millets? What % of their food plate are millets? All these need to be explored before drawing conclusions. It's not surprising that households with high coarse cereals consumption have high wasting and malnutrition. To assume that the underlying cause of wasting is coarse cereals (and that wasting would be less without coarse cereals) seems erroneous and perhaps indefensible. Comparing similar households with and without coarse cereal consumption could be a convincing way to draw conclusion in the present manuscript.

4. Why have the authors excluded Ragi (finger millets) from the analysis, which is one of the most nutritious millets?

5. With Public distribution system (PDS), a food security program in India distributing majorly rice and wheat throughout the country at subsidized rates, it might be difficult to conclude that the millet growing communities, who have access to PDS are only consuming millets and hence have poor nutritional status?

6. The authors mention that at 6 months, the wasting in children is the highest, does the data say that disaggregated data on millet cultivation and wasting at 6 months has the most significant association?
7. It is somewhat worrisome to see the concluding line stating that "Policies and programs targeting malnutrition need to address type of cereal consumed in order to impact childhood malnutrition in parts of India where subsistence cultivation of millets for staple consumption is prevalent." The millet consumption can actually add diversity to the Indian diets and the presence of anti-nutrients can be assessed in the light of anti-nutrient and micronutrient molar ratio (e.g. phytate: iron molar ration before concluding that the millets can lead to malnutrition.

Recommendation: In its current state, this manuscript may be rejected.

Is the work clearly and accurately presented and does it cite the current literature?  
No

Is the study design appropriate and is the work technically sound?  
No

Are sufficient details of methods and analysis provided to allow replication by others?  
Yes

If applicable, is the statistical analysis and its interpretation appropriate?  
No

Are all the source data underlying the results available to ensure full reproducibility?  
Yes

Are the conclusions drawn adequately supported by the results?  
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Food systems research, assessment of nutritional status, nutrient analysis, nutritional status of indigenous communities of India

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 09 Oct 2020

Prashanth N Srinivas, Institute of Public Health Bengaluru, Bengaluru, India

Thank you for your careful review of our submission and for raising important concerns. We have now comprehensively revised the paper and hope that the revised version has adequately responded to your concerns raised. We first provide a comprehensive overview of the main arguments underlying our revision and subsequently provide point-by-point response to the specific concerns raised. We kindly point you to review substantive responses we have made in response to reviewer 1 under the following headings which are also relevant to concerns raised by you: (a) On protein and amino acid content of cereals, (b)
On the matter of why some cereals such as millet and sorghum have lower digestibility, (c) Protein quality in the first 1000 days of conception, (d) On the micronutrient content in cereals

On the choice of title: There have been questions linked to our choice of the title by both reviewers. Overall, there are 108 districts each with higher prevalence of stunting and wasting, with an overlap of both in 18 districts (Figure 1 showing overlaps between two sets of districts in response to reviewer 1). Undeniably, cereals constitute upwards of 70% protein consumption in rural India and malnutrition has a strong rural preponderance worldwide\(^1,2,3\). Looking from the prism of predominantly cereal based diets, the wide range of protein (or amino acid) and micronutrient availabilities among cereals (as explained in our overarching response above) could well determine both wasting and stunting. Furthermore the results provided in the revised version strengthen the evidence-base for an association of wasting and low BMI with millet cultivation (as a proxy for consumption).

On the hypothesis: Our hypothesis is based on the distinct patterns of higher prevalence of stunting and wasting as well as the wide diversity in the cultivation and nutritional values of both micronutrients and proteins among cereals. We agree that other factors linked to poverty like dietary diversity, infections, low birth weight could well be contributing to malnutrition. This emphasizes a need for well-designed studies to look for the contribution of cereals consumed to the patterns of malnutrition. But, given that some states with higher poverty (e.g., UP and Bihar) with relatively lower levels of low BMI and wasting than states in peninsular (or central) India (also see Table 1 in response to Reviewer 1 and the section titled On the early onset of malnutrition in India and ecogeographic patterns & section titled On the micronutrient content of cereals) points to other factors.

On the exclusion of ragi (finger millet): As mentioned in the text we excluded ragi from the millets because of its purported nutritional richness and its distinct subfamily in the grass family Poaceae\(^4,5,6\). This is also corroborated by patterns in the African continent where the countries which had the highest production of ragi (Uganda and Tanzania) are in the highlands of East Africa with lower prevalence of wasting when compared to other millet-growing regions in the continent\(^4,7\). The figure showing the distribution of Ragi in eastern highlands is available from p.42 (Link); the geo-spatial analysis of prevalence of malnutrition in low- and middle-income countries by Kinyoki et al. figure 2 showing low prevalence of wasting in areas having predominant ragi cultivation is available (Link).

About Poverty, PDS and food security in India and its effects on our findings (see table uploaded on Figshare as tables are not allowed in response to reviewers): That the Public Distribution system (PDS) is invaluable in managing food security in the country is undeniable. The share of rice or wheat consumption from PDS in different states indicates that the percentage is quite less (ranging from 7.6% in Gujarat to 34.3% in Chhattisgarh). The percentage of improvement in PDS use from 2004-5 to 2011-12 has not led to a commensurate decline in undernutrition in the country\(^8,9\). Moreover, the coverage of PDS is much higher in hill-states of northern India and in South Indian states as compared to other regions where malnutrition prevalence is higher\(^9\). Hence, the likelihood of effects of PDS especially in the regions that we analyse in this paper by the marginal farmers and rural poor is likely to be low with subsistence cultivation continuing to play an important part, especially among the poorest communities.
**About validity of data for study purposes:** The major nutrition surveys completed in this decade are summarised by Rathi et al. (see table 1; Link to journal). The Comprehensive National Nutrition Survey 2016-18 has data by state and their respective urban/rural areas and not by districts. The district level household survey 4 (DLHS4 in 2012-14) covered only 336 districts among 640 present at that time. The minimum disaggregation available on such a scale is at the district level only. The malnutrition data in our study was extracted from NFHS4 which is a nationwide survey encompassing all districts. The Hemalatha et al. study uses multiple data inputs with the latest being NFHS4 and India Urban Nutrition Survey Data 2015-2016. As seen from table 4 above taken from Rathi et al. NFHS4 is the only nationwide survey encompassing all districts completed in the present decade. The food consumption data too has dietary groups with cereals aggregated in a group, as grains, roots and tubers. For the purposes of our study we needed separate consumption of cereal (by type) in each district which is not available in CNNS or NFHS4. The older NSSO (NSS 55) has data on type of cereals consumed but that too is not available by district but by 77 ecogeographic zones.

**Point-by-point response to review observations**

- **Title:** The title has issues in terms of including food (cereals) and nutrients (proteins and micronutrients) in the same basket, which is not clear.

  Thank you for bringing the title to attention. We have explained above under the heading “on the choice of the title”.

- **Hypothesis:** According to the manuscript, families depending on subsistence farming and growing millets may have higher levels of wasting in under 5 children and malnourishment in women. Assessing causality by relating production of millets to nutritional status without looking at actual consumption and other factors [underlying and basic factors (ref to UNICEF conceptual framework of Causes of maternal and child malnutrition)] may be flawed.

  We accept that obtaining actual consumption would have been ideal for establishing or negating such a hypothesis. In the version 2 of our paper, we have attempted to include other factors pertinent to malnutrition (available through nationwide surveys) in our analysis. We have explained this in detail under the sections On the hypothesis and On the validity of data for study purposes. Please also see the more extended multivariate analysis in version 2.

- **The issue of assuming causality from correlations with perhaps erroneous conclusions is a major concern in this manuscript.** It is crucial to look at dietary consumption data, from NSSO and NNMB and it is also important to adjust for all the other factors like SES, endemicity to diseases, access to potable water before superimposing millet cultivation and prevalence of malnutrition in women and wasting in children. These communities are poverty stricken and have limited access to several resources mentioned above. So the yield of crop is questionable as well. What % of their farming are millets? What % of their food plate are millets? All these need to be explored before drawing conclusions. It's not surprising that households with high coarse cereals consumption have high wasting and malnutrition. To assume that the underlying cause of wasting is coarse cereals (and that wasting
would be less without coarse cereals) seems erroneous and perhaps indefensible. Comparing similar households with and without coarse cereal consumption could be a convincing way to draw conclusion in the present manuscript.

We have strengthened the analysis in the revised version as well has edited the language implying causality. We, in fact do not want to attribute causality but wish to describe a consistent pattern and provide a plausible hypothesis in the epidemiology of malnutrition in India. Hence, we have placed the pathway incorporating the mechanisms of causation in discussion rather than results in version 2. We have incorporated few of the variables pertaining to causation of malnutrition in a multivariate analysis as well. Dietary consumption data from nationwide surveys have limitations as mentioned under the section About validity of data for study purposes. We concede that well designed field studies are required to come to a clear position on this issue.

- Why have the authors excluded Ragi (finger millets) from the analysis, which is one of the most nutritious millets?

We have dwelt on this under the above section titled On the exclusion of ragi(finger millet).

- With Public distribution system (PDS), a food security program in India distributing majorly rice and wheat throughout the country at subsidized rates, it might be difficult to conclude that the millet growing communities, who have access to PDS are only consuming millets and hence have poor nutritional status? This has been explained in the section above titled About Poverty, PDS and food security in India and its effects on our findings.

- The authors mention that at 6 months, the wasting in children is the highest, does the data say that disaggregated data on millet cultivation and wasting at 6 months has the most significant association?

In Fig 5 of version 1 and Figs 9 & 10 of version 2 the age profile of children in the 108 high stunting and 108 high wasting districts is plotted. The districts with higher wasting (which have higher cultivation of millets as brought out in the results) have higher wasting at 6 months. However, data are unavailable to establish this at the household level due to lack of data on type of cereal consumed (which we have elaborated under the discussion).

- It is somewhat worrisome to see the concluding line stating that "Policies and programs targeting malnutrition need to address type of cereal consumed in order to impact childhood malnutrition in parts of India where subsistence cultivation of millets for staple consumption is prevalent." The millet consumption can actually add diversity to the Indian diets and the presence of anti-nutrients can be assessed in the light of anti-nutrient and micronutrient molar ratio (e.g. phytate: iron molar ratio before concluding that the millets can lead to malnutrition.

We have indeed taken note of this suggestion and changed the manuscript in version 2 accordingly. We have taken into consideration the diversity of nutritional profiles of various cereals and brought out tables (Table 3 & 4) to highlight this. Further detailed explanation
has been given under the headings On protein and amino acid content of cereals, Protein quality in the first 1000 days of conception and On the micronutrient content in cereals in the response to reviewer 1. The concluding line as stated in the comment has been removed in version 2.

References:


**Competing Interests:** None declared

Reviewer Report 21 July 2020

https://doi.org/10.21956/wellcomeopenres.17478.r39353

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Edward J.M. Joy

Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, UK

The authors assess whether staple cereal consumption patterns in India underlie malnutrition patterns. They test this through an association between District-level production of staple cereals, and prevalence of stunting/wasting in children or low BMI/short stature in adult women.

The article is quite clearly written and I appreciate that the authors have made the datasets and analysis code available for reviewers/readers. This is commendable.

However, there are a number of areas that concern me about the study:

The study title calls this an exploratory analysis, and if this is to be indexed I think the interpretation of the results and framing of the whole paper needs to be consistent with this. For example, the authors currently write "Policies and programs targeting malnutrition need to address type of cereal consumed in order to impact childhood malnutrition in parts of India where subsistence cultivation of millets for staple consumption is prevalent". I don't think such a statement is justified based on the findings of this paper, given the exploratory nature of the analysis, quite apart from the methodological shortcomings.

The title also specifies wasting, where 4 different anthropometric outcomes were assessed.

There are several methodological shortcomings to the analysis, in my opinion. The following shortcomings are noted by the authors:

1. Cereal production is not equivalent to cereal consumption, so testing the hypothesis using cereal production data is problematic. Can the authors explain why 'consumption' data were not used, e.g. from the Comprehensive National Nutrition Survey?

2. Data are integrated at the District-level. This level of aggregation is likely to mask the true
effect, if there is indeed an effect, between millet consumption and risk of malnutrition. The following shortcomings are not reported in the paper:

- The authors propose a biochemical pathway through which consumption of millets and sorghum might negatively affect nutritional status of women and children. However, they ignore wider contextual factors that are likely to be related both to the likelihood of producing millets and to the risk of malnutrition. These factors include, for example, socioeconomic status and likelihood of drought. There are multiple pathways linking such environmental and socioeconomic factors to nutritional status, mostly operating outside specific biochemical pathways. The proposed pathways (Figure 6) should at most be included in the discussion (not results), with acknowledgement that it may explain a small proportion of the observed association...if at all.

- The relationship between millet production and prevalence of malnutrition outcomes (displayed in Figures 3 & 4) is messy. This is not necessarily inconsistent with the hypothesis, considering the District-level nature of the data and the multiple and complex factors underlying nutritional status. However, do the authors really find sufficient evidence with appropriate statistical certainty to reject the null hypothesis, that there is no association between the independent and dependent variables? The authors need to present a more comprehensive assessment of the associations they find, including appropriate p-values. NB I found this hard to review as the statistical test of association was not specified in the methods. Relatedly, the axes in Figures 3 & 4 need units.

- As above, assuming production closely predicts consumption is a major limitation of the study. But this could be partially addressed through limiting the analysis to rural households only. This might avoid any associations being driven by highly-urban Districts where there is both low millet production and better-than-average nutritional status.

- The authors pick out particular micronutrients and amino acids which are apparently lower in concentration or bioavailability in millets than in other staple cereals, and suggest this offers a mechanism which might underlie the observed associations. I am not clear how the authors came to select these micronutrients and amino acids. There are others, for example calcium, which are present at much greater concentrations in millets (especially finger millet) than other staple cereals. The idea that a diet with greater millet consumption is less nutritious is not supported by the evidence.

Other comments:


From visual analysis of the figures, it appears there are some discrepancies. The authors could discuss this.

- The pattern of increased stunting and wasting prevalence around 12 mo of age (Figure 5) is consistent with other settings and is likely due to poor IYCF practices and high rates of diarrhoea when moving from exclusive breastfeeding to complementary feeding.

- The authors could consider using a different base colour for Figure 1. The current colouring might not translate well to presentations or black and white printing. Also, the hatched areas represent areas with 'higher prevalence' of stunting or wasting, but it's not clear what they are higher than, i.e. what's the comparator. Overall, I suggest the authors re-consider the framing of the paper and presentation of findings.
References

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
No

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
No

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
No

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Dietary micronutrient assessment, population micronutrient assessment

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 09 Oct 2020

Prashanth N Srinivas, Institute of Public Health Bengaluru, Bengaluru, India

Comments of Dr Joy

Thank you for your careful review of our submission and for raising important concerns. We have now comprehensively revised the paper and hope that the revised version has adequately responded to your concerns raised. We first provide a comprehensive overview of the main arguments underlying our revision and subsequently provide point-by-point response to the specific concerns raised.

**On protein and amino acid content of cereals:** Cecily D Williams, in her pathbreaking description of Kwashiorkor in 1933 commented\(^1\): “*As maize is the only source of supplementary food, some amino acid or protein deficiency cannot be excluded as a cause.*” The understanding about proteins being relevant to the causation of stunting and Intrauterine
growth restriction (IUGR) through the MTOR pathway has been extensively studied\(^2,3,4,5\).
Since proteins are absorbed through the ileum after breakdown into amino acids or short peptide chains, and, MTOR being exquisitely sensitive to amino acids, we incorporate the MTOR pathway in hypothesizing about the purported differences in wasting prevalence between northern and peninsular India (see figure 1). Further, as per the 2011 FAO Expert Consultation on Protein Quality Evaluation in Human Nutrition\(^6\), it is recommended that “dietary amino acids be treated as individual nutrients and that wherever possible data for digestible or bioavailable amino acids be given in food tables on an individual amino acid basis”.

Due to paucity of human data it was further stated that “Where human data are lacking it is recommended that true ileal amino acid digestibility values from the growing pig be used, and where these data are not available from the growing laboratory rat.”\(^6\) This consideration is underlying our use of ileal digestibility data in pig (Table 5 in the revised version). In a recent paper Swaminathan, Vaz & Kurpad while analysing protein intakes in India\(^7\), highlight lower protein quality of a predominantly cereal based rural and tribal diet, particularly in pregnancy. There are small but significant differences in the Lysine contents across cereals in their analysis (table2 in Swaminathan S et al\(^7\)). This is in line with earlier more global evidence-base\(^8\). These differences are germane to the differences in malnutrition patterns between northern and peninsular India.

On the matter of why some cereals such as millet and sorghum have lower digestibility, Millward implicates tougher plant cell walls prevalent in millets; others have implicated anti-nutrient factors as well\(^8,9,10,11\). This is corroborated by measures such as the Digestible indispensable amino acid scores (DIAAS) of cooked cereals (including rice and wheat) which are the lowest for foxtail and proso millet\(^12\). Other independent analyses to determine the standardised ileal digestibility (SID) among eight cereal grains using DIAAS scores also have shown highest values for rice but the lowest for maize, rye and Sorghum\(^13\). Furthermore, excess Leucine in Sorghum has been implicated in Pellagra reported among people who consume Sorghum as a staple in India\(^14\). There are few studies that compare ileal digestibility across various complementary foods in India. In a comparison of standardized ileal digestibility(%) of amino acids between Sorghum, pearl millet and different varieties of corn, Sorghum was the lowest followed by pearl millet. The different corn varieties were higher than both\(^15\). The digestibility of pearl millet protein has been suspected to be less than other major grains\(^16\). While evaluating the protein quality of complementary foods using dual isotope tracer method in comparing the true ileal digestibility of rice, finger millet (ragi) and egg, finger millet and mung dal had the lowest\(^13\). Studies are ongoing for other millets but are currently unavailable (email communication with corresponding author\(^17\)).

**Protein quality in the first 1000 days of conception.** Pregnant women in fact need an additional 1, 9 and 31 gm per day in first, second and third trimester respectively\(^18\). This lack of protein (and energy quality) is linked to low maternal BMI and Intrauterine growth restriction\(^18\). As per the standard FAO reference source on millets and sorghum, Lysine amino acid score of pearl millet is variable (26-69)\(^8\). Barnyard millet, little millet and Sorghum had the lowest Lysine scores among millets\(^8\). The lower glycaemic index of millets vis-à-vis rice and wheat (which is indeed beneficial for elderly Diabetics), on the other hand for pregnant women on pre-dominant millet-based diet could contribute to low birth weight and wasting since glucose along with amino acids is an important upstream regulator for
MTOR⁴.¹⁹. In fact the FAO asserts that exclusive millet diets are not adequate to meet the growth requirements of infants and young children⁸. In table 5 (of the revised version of our paper) we provide Lysine scores of cereals and their references in studies conducted in University of Illinois, Urbana-Champaign and elsewhere. The table is extracted from a compendium curated by Hans-Henrik Stein from published data.

Based on these arguments and evidence presented in our paper further supported by extensive published data, we submit that monotonous cereal based diets of the rural poor wherever they are not supplemented with good quality protein from other sources could drive wasting, as is seen in monotonous millet-based diets.

**On the micronutrient content in cereals:** Micronutrient availability in rice and wheat, on the contrary, is worse off than in millets (see table 6 of revised paper). This could be underlying the higher prevalence of stunting in rice and wheat growing areas of northern India (possibly related to Zinc deficiency). Review evidence too corroborates the other reviewer’s observation that high phytate and phytate to mineral molar ratios in plant based diets as contributing to deficiencies of Iron, zinc and Calcium²⁰,²¹,²²,²³. The higher Iron, Zinc and Calcium content in millets (especially pearl millet, Sorghum and other millets) could be offsetting the phytate and phenol inhibitors in comparison to rice and wheat (Table 6 data from Indian Food Composition Table 2017²⁴). This underlies our assertion “Lower lysine, high phytates with lowered micronutrients like zinc and iron in cereal based diet in wheat and rice growing areas with poor dietary diversity could lead to stunting” (as per caption of pathway figure in version 1; now figure 11). Zinc has a known association with linear growth and supplementation in developing countries has been beneficial in marginal gain of length²⁵,²⁶. There has been a decline in the zinc & Iron molar ratios with phytates, in India over the last four decades, attributed to lesser consumption of millets and sorghum²¹,²².

Characterising micronutrient availabilities in vivo (particularly Zinc, Vitamin D, Magnesium, Phosphate, Selenium) in different cereal based meals will require state-of-the-art laboratory techniques like stable isotope studies. Iodine is another micronutrient critical for foetal and child growth, but, unlikely to be of consequence in view of universal Iodization of common salt in India. Iodine availability of different cereals is however unavailable in IFCT 2017.

Malnutrition prevalence related to micronutrients are available only at state level and with no district level data and have been compiled by us from different sources in table 1 below. The state-level data do not reproduce intuitive patterns. For example, poorer states (higher poverty rates) are better off with respect to prevalence of low BMI among women in 10-19 years age group when compared with richer states which report higher coarse cereal cultivation (Rajasthan, Maharashtra, Karnataka and Gujarat highlighted in red). Similarly, lesser degree of low zinc prevalence was seen in 1-4 year age groups in Rajasthan and Maharashtra (see discussion above on better off micronutrient profile of coarse cereals) in comparison to Uttar Pradesh and Bihar. However, these patterns are not consistent (for example Karnataka which reports higher low zinc prevalence in 1-4 year age group despite having relatively high coarse cereal consumption). Nevertheless, a study comparing zinc levels among preschool children across five states of India too showed higher prevalence in Orissa(51.3%) followed by Uttar Pradesh(48.1%), Gujarat(44.2%), Madhya Pradesh(38.9%) and Karnataka(36.2%)²⁷. The latter three have a higher production of coarse cereals in comparison to others as seen in the table (since tables are not allowed here, this table
On the early onset of malnutrition in India and ecogeographic patterns: The timing of onset of malnutrition in India has been reported in earlier studies. The paper titled *The Asian Enigma* by UNICEF in 1996 brought it to the forefront with a discussion about higher proportion of low birth weights in India (and Bangladesh) with its linkages to women’s health in general and maternal nutrition in particular. Cesar Victora et al. have demonstrated this with India having the lowest weight for age Z scores at 1 month of age. This aspect was emphasized by Martorell et al. in the comparisons between stunting and wasting prevalence as well as their respective age of occurrence between India and Guatemala. Figure 1 in the paper by Martorell illustrates this comparison indicating earlier onset of wasting in India.

In our analysis the stunting prevalence comparison between the districts with high stunting and high wasting showed a similar pattern as seen in figures 9 and 10 (in the revised version), with higher and earlier onset of wasting in the 108 high wasting districts. That is likely to be attributable to maternal nutritional factors during pregnancy, lactation and low birth weight. However, granular data on low birth weight by district in India not being available, this remains a hypothesis to be tested when better data becomes available.

Further evidence of ecogeographic patterning of malnutrition is also available in the landmark Lancet 2008 series on malnutrition where it is asserted “Furthermore, stunting and severe wasting are not necessarily associated on a geographical or ecological basis—ie, countries with a similar stunting prevalence can have a several-fold difference in the prevalence of severe wasting.” This phenomenon has also been written about by Cesar Victora in 1992. What we are attempting to posit here is that, in a diverse country like India, such differences are likely to be important in addressing malnutrition.

Point-by-point response to review observations
- The authors assess whether staple cereal consumption patterns in India underlie malnutrition patterns. They test this through an association between District-level production of staple cereals, and prevalence of stunting/wasting in children or low BMI/short stature in adult women. The article is quite clearly written and I appreciate that the authors have made the datasets and analysis code available for reviewers/readers. This is commendable.

Thank you.

- The study title calls this an exploratory analysis, and if this is to be indexed I think the interpretation of the results and framing of the whole paper needs to be consistent with this. For example, the authors currently write "Policies and programs targeting malnutrition need to address type of cereal consumed in order to impact childhood malnutrition in parts of India where subsistence cultivation of millets for staple consumption is prevalent". I don't think such a statement is justified based on the findings of this paper, given the exploratory nature of the analysis, quite apart from the methodological shortcomings. The title also specifies wasting, where 4 different anthropometric outcomes were assessed.

There have been questions linked to our choice of the title by both reviewers. Overall, there
are 108 districts each with higher prevalence of stunting and wasting, with an overlap of both only in 18 districts (see Junaid et. al.; reference number 33). Undeniably, cereals constitute upwards of 70% protein consumption in rural India and malnutrition has a strong rural preponderance worldwide\textsuperscript{7}. Looking from the prism of predominantly cereal based diets, the wide range of protein (or amino acid) and micronutrient availabilities among cereals (as explained in our overarching response above) could well determine both wasting and stunting. Furthermore the results provided in the revised version strengthen the evidence-base for an association of wasting and low BMI with millet cultivation (as a proxy for consumption).

- There are several methodological shortcomings to the analysis, in my opinion. The following shortcomings are noted by the authors: Cereal production is not equivalent to cereal consumption, so testing the hypothesis using cereal production data is problematic. Can the authors explain why ‘consumption’ data were not used, e.g. from the Comprehensive National Nutrition Survey? Data are integrated at the District-level. This level of aggregation is likely to mask the true effect, if there is indeed an effect, between millet consumption and risk of malnutrition. This is an important shortcoming of the paper. However, no consumption data are currently available. Detailed explanation for this is provided in response to reviewer 2 under the heading *About validity of data for study purposes*.

- The following shortcomings are not reported in the paper: The authors propose a biochemical pathway through which consumption of millets and sorghum might negatively affect nutritional status of women and children. However, they ignore wider contextual factors that are likely to be related both to the likelihood of producing millets and to the risk of malnutrition. These factors include, for example, socioeconomic status and likelihood of drought. There are multiple pathways linking such environmental and socioeconomic factors to nutritional status, mostly operating outside specific biochemical pathways. The proposed pathways (Figure 6) should at most be included in the discussion (not results), with acknowledgement that it may explain a small proportion of the observed association...if at all.

We agree with the reviewer observation about the need to integrate other known co-variates of malnutrition which is now done in version 2. Furthermore as suggested the implications of our findings are moved to the discussion (figure 11 relating to plausible pathways is now moved to discussion).

- The relationship between millet production and prevalence of malnutrition outcomes (displayed in Figures 3 & 4) is messy. This is not necessarily inconsistent with the hypothesis, considering the District-level nature of the data and the multiple and complex factors underlying nutritional status. However, do the authors really find sufficient evidence with appropriate statistical certainty to reject the null hypothesis, that there is no association between the independent and dependent variables? The authors need to present a more comprehensive assessment of the associations they find, including appropriate p-values. NB I found this hard to review as the statistical test of association was not specified in the methods. Relatedly, the axes in Figures 3 & 4 need units.

Thank you for these observations. We have now reported the details of our statistical analysis. Corresponding changes have also been made in erstwhile figures 3 and 4 which
have now been broken up into figures 3-5 & 6-8 in the revised version along with appropriate p-values.

○ As above, assuming production closely predicts consumption is a major limitation of the study. But this could be partially addressed through limiting the analysis to rural households only. This might avoid any associations being driven by highly-urban Districts where there is both low millet production and better-than-average nutritional status.

The multivariate analysis has now taken into the account the effect of rural population proportion in the district.

○ The authors pick out particular micronutrients and amino acids which are apparently lower in concentration or bioavailability in millets than in other staple cereals, and suggest this offers a mechanism which might underlie the observed associations. I am not clear how the authors came to select these micronutrients and amino acids. There are others, for example calcium, which are present at much greater concentrations in millets (especially finger millet) than other staple cereals.

This has now been comprehensively addressed in our overarching response above (see particularly discussion under sub-heading On the matter of why some cereals such as millet and sorghum have lower digestibility and On micronutrient availability in cereals. Please see also section On the exclusion of ragi in response to reviewer 2).

○ The idea that a diet with greater millet consumption is less nutritious is not supported by the evidence.

This has been addressed in the revisions made. Please also refer to section above titled On micronutrient availability in cereals.


Hemalatha et al. have used multiple data sources for their analysis, of which the only comprehensive dataset that comprises district-level malnutrition data for the entire country is NFHS4 (which we have used in our analysis). Other datasets used in their paper do not provided district-level data for the entire country. Our estimates of malnutrition prevalence at the district level are reproducible and are consistent with analysis of NHFS4.

○ From visual analysis of the figures, it appears there are some discrepancies. The authors could discuss this.

The maps have been reproduced with better contrast and legends for clarity. The few instances of lack of overlaps between millet cultivation and wasting (e.g., bajra in north India) are now discussed in the revised version.

○ The pattern of increased stunting and wasting prevalence around 12 mo of age (Figure 5) is consistent with other settings and is likely due to poor IYCF practices and high rates of diarrhoea when moving from exclusive breastfeeding to complementary feeding.

We have extensively discussed the early onset of malnutrition in India above.

○ The authors could consider using a different base colour for Figure 1. The current
colouring might not translate well to presentations or black and white printing. Also, the hatched areas represent areas with 'higher prevalence' of stunting or wasting, but it's not clear what they are higher than, i.e. what's the comparator.

Thank you for these suggestions. The revised figures address these concerns. We took the levels of districts having higher prevalence of stunting >45% and wasting >27% based on cut-offs suggested by Junaid et al article\textsuperscript{33}. We used levels of > = 30% and >= 15% as high prevalence of women’s BMI (<18.5) and short stature(< 145 cms) respectively.

References:


15. Digestible energy and amino acid contents in Canadian varieties of sorghum, pearl
24. Indian Food Composition Tables 2017 T. Longvah, R. Ananthan, K. Bhaskarachary and K. Venkaiah


**Competing Interests:** Nil