Jones, A. D., Hayter, A. K. M., Baker, C. P., Prabhakaran, P., Gupta, V., Kulkarni, B., ... Kinra, S. (2016). The co-occurrence of anemia and cardiometabolic disease risk demonstrates sex-specific sociodemographic patterning in an urbanizing rural region of southern India. European Journal of Clinical Nutrition, 70(3), 364-372. DOI: 10.1038/ejcn.2015.177

The co-occurrence of anemia and cardiometabolic disease risk demonstrates sex-specific sociodemographic patterning in an urbanizing rural region of southern India

Andrew D. Jones[1], Arabella K.M. Hayter[2], Chris P. Baker[2], Poornima Prabhakaran[3], Vipin Gupta[4], Bharati Kulkarni[5], George Davey Smith[6], Yoav Ben-Shlomo[7], K.V. Radha Krishna[5], P. Uday Kumar[5], Sanjay Kinra[2]

[1]School of Public Health, University of Michigan, Ann Arbor, MI, USA

[2]Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

[3]Public Health Foundation of India, New Delhi, India

[4]Department of Anthropology, University of Delhi, New Delhi, India

[5]National Institute of Nutrition, Indian Council for Medical Research, Hyderabad, India

[6]MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK

[7]School of Social and Community Medicine, University of Bristol, Bristol, UK

Corresponding author and author from whom reprints may be requested:
Andrew D. Jones; 3846 SPH I, 1415 Washington Heights, Ann Arbor, MI 48109; phone: 734.647.1881; fax: 734.763.5455; jonesand@umich.edu

Running title: Nutritional double burden in India

List of abbreviations: Analysis of variance (ANOVA); Andhra Pradesh Children and Parents Study (APCAPS); Body mass index (BMI); Confidence interval (CI); Defense Meteorological Satellite Program – Operational Linescan System (DMSP-OLS); Dual Energy X-Ray Absorptiometry (DXA); Genetics and Biochemistry Laboratory of the South Asia Network for Chronic Disease (GBL); Hyderabad Nutrition Trial (HNT); Integrated Child Development Services (ICDS); Low- and middle-income countries (LMICs); National Institute of Nutrition, Hyderabad (NIN); Metabolic syndrome (MetS);

National Center for Health Statistics (NCHS); Night-time light intensity (NTLI); Odds ratio (OR)

Sources of financial support: The Hyderabad Nutrition Trial (1987-1990) was funded by the Indian Council of Medical Research and the United States Agency for International Development (PI: KV Rameshwar Sarma). The third wave of data collection for the APCAPS study was funded by the Wellcome Trust (Grant: 084674/Z; PI: S Ebrahim). The National Institute of Nutrition (Indian Council of Medical Research) provided infrastructural support. PhD studentships were funded by the Wellcome Trust (Grant: 084754; P Prabhakaran), World Bank (M Matuzaki) and Bloomsbury consortium (T Sorensen) and a Research fellowship was funded by the Wellcome Trust (Grant: 084754; R Pant). The funders had no role in study design, data collection, analysis, decision to publish, or preparation of the manuscript.

Conflicts of interest: The authors have no conflicts of interest to declare.

Abstract

Background/Objectives: To determine the extent and sociodemographic determinants of anemia, overweight, metabolic syndrome (MetS), and the co-occurrence of anemia with cardiometabolic disease risk factors among a cohort of Indian adults.

Subject/Methods: Cross-sectional survey of adult men (n=3,322) and non-pregnant women (n=2,895) aged 18 y and older from the third wave of the Andhra Pradesh Children and Parents Study that assessed anemia, overweight based on Body Mass Index, and prevalence of MetS based on abdominal obesity, hypertension, and blood lipid and fasting glucose measures. We examined associations of education, wealth and urbanicity with these outcomes and their co-occurrence.

Results: The prevalence of anemia and overweight was 40% and 29% among women, respectively, and 10% and 25% among men (P<0.001), respectively, while the prevalence of MetS was the same across sexes (15%) (P=0.55). The prevalence of concurrent anemia and overweight (9%), and anemia and MetS (4.5%) was highest among women. Household wealth was positively associated with overweight and MetS across sexes (P<0.05). Independent of household wealth, higher education was positively correlated with MetS among men (OR (95% CI): MetS: 1.4 (0.99, 2.0)) and negatively correlated with MetS among women (MetS: 0.54 (0.29, 0.99)). Similar sex-specific associations were observed for the co-occurrence of anemia with overweight and MetS.

Conclusion: Women in this region of India may be particularly vulnerable to co-occurring anemia and cardiometabolic risk, and associated adverse health outcomes as the nutrition transition advances in India.

Keywords: anemia, metabolic syndrome, nutrition transition, double burden, India

Introduction

Global diets have transformed dramatically over the past three decades. In recent years, this nutrition transition, characterized by a convergence of diets toward increased intakes of vegetable oils, refined and processed foods, and added sugars as well as a shift away from consumption of coarse grains and legumes, has occurred most rapidly in low- and middle-income countries (LMICs)[1]. These dietary changes, often decoupled from economic development, have contributed to a precipitous rise in the prevalence of obesity and associated cardiometabolic disease[2]. This has led to an emerging "double burden" of malnutrition in many LMICs wherein persistent conditions of poverty and poor environmental sanitation continue to contribute to undernutrition (e.g., underweight, linear growth faltering, and associated nutritional disorders) among substantial proportions of the population[3]. This nutritional double burden has been observed in many countries including in India where more than one-third of women of childbearing age (15-49 y) are underweight (36%) and nearly one in seven are overweight or obese (13%)[4]. The prevalence of cardiometabolic disease risk often tracks closely with the increasing prevalence of obesity[5]. In India, for example, as many as one-fifth to one-third of adults in urban regions[6-8], and one in ten adults in rural populations[9] have developed the metabolic syndrome (MetS), a multi-component risk factor that is associated with increased morbidity and mortality, especially from cardiovascular disease[10].

Yet, this nutritional double burden is not limited to the co-occurrence of undernutrition and obesity among populations. Individuals who are obese or have other risk factors of cardiometabolic disease may be simultaneously undernourished, experiencing micronutrient deficiencies and associated disorders (e.g., anemia) despite consuming sufficient, or excess, dietary energy[11]. Anemia is of particular concern when characterizing the undernutrition component of this individual-level nutritional double burden for several reasons: 1) anemia often reflects a deficiency of one or more micronutrients (e.g., iron, folic acid, vitamin A)[12], 2) these nutrients may be lacking in diets dominated by refined and processed foods[13], 3) overweight may not only co-occur with these deficiencies, but for iron deficiency in particular, may in fact exacerbate the deficiency through inflammation-mediated sequestration of irons stores and inhibited absorption[14-16], and 4) anemia remains a considerable public health concern in most LMICs, especially among women and young children[17]. In India, more than one half of women of childbearing age are anemic (56%) as are nearly three quarters of preschool-aged children (70%)[4].

The extent and determinants of the co-occurrence of anemia, overweight and other risk factors of cardiometabolic disease within individuals have not been adequately studied. In India in particular, the co-occurrence of overweight and underweight has been examined at national and sub-national levels[18-20], yet individual-level double burden manifestations have received little attention. Furthermore, across most world regions, there is little information about sex differences in the extent and determinants of the double burden and its underlying conditions[21]. Given the persistence of nutritional anemia as a public health concern in India as in most LMICs, the concomitant increase in overweight among the same vulnerable populations, and the associated increased risk of morbidity and mortality from both anemia and excessive adiposity, there is a critical need to understand the extent and sociodemographic determinants of this double burden in order to develop coherent policy solutions to confront it.

The objective of this study is: 1) to determine the extent of anemia, cardiometabolic disease risk, and the co-occurrence of these conditions among a cohort of adults in an urbanizing rural region of southern India, and 2) to determine the associations of these conditions with sociodemographic characteristics including education, income, and urban environment. We hypothesize that vulnerability to the individual-level nutritional double burden and its underlying conditions will be greatest among women and that there will be sex-specific patterning of the sociodemographic determinants of these conditions.

Subjects and Methods

Study design and population

The Andhra Pradesh Children and Parents Study (APCAPS) is an intergenerational cohort, established to follow up the participating households of the Hyderabad Nutrition Trial (HNT), a population-based evaluation of India's Integrated Child Development Services (ICDS) scheme. The HNT trial was carried out in 1987-90 among 29 villages in two adjacent administrative areas, called "blocks", approximately 50-100 km from the city of Hyderabad in southern India[22]. Villages were randomly selected for participation based on geographic location within each of the two blocks (i.e., contiguous villages within a 10 km radius of the block's central village). Fifteen villages were selected in the block where the ICDS scheme was already in place (intervention arm), and 14 villages were selected in the block where the scheme was awaiting implementation (control arm). An initial follow-up of the mothers and children of the HNT birth cohort was carried out in 2003-05 with subsequent waves of data collection in 2009-10 and 2010-12. We examined cross-sectional data from the third and most recent wave of the APCAPS study which included not only HNT trial children, but also the parents and siblings of these children. A complete description of the APCAPS cohort including details regarding the initial HNT trial and all follow up data collection has been published previously[23].

Variables and measurement

The body mass index (BMI) (kg m^{-2}) of each participant was calculated based on weight and height measurements. We used adjusted BMI cut-offs for Asian populations (i.e., overweight: ≥23 and <25 kg m^{-2}; obese: ≥25 kg m^{-2}) to define overweight and obesity[24, 25] based on the increased risk of adverse metabolic consequences among Asians at lower BMI thresholds[26]. Waist circumference was measured by non-stretch metallic tape. Because there are no globally recognized values for defining adult "stunting", we defined it, similar to several previous studies, based on the National Center for Health Statistics (NCHS) reference at 18 y [27, 28]. Standing height <163.6 cm for men and <151.8 cm for women, that is, < -2 Z-scores below the NCHS reference, were used to define adult stunting[29].

Fat mass was also assessed by Dual Energy X-Ray Absorptiometry (DXA) (Hologic models Discovery A or 4500W, Bedford, MA, USA) in a subsample of participants who self-selected to participate in DXA measurement. A whole body scan was performed with the participant supine on the scanning bed with their arms resting by their sides. Standard Hologic software options were used to define regions of the body (i.e., head, arms, trunk, and legs). We calculated total body fat based on the fat mass of each body region as a percentage of total body mass. Though clear cut-offs for defining obesity based on body fat percentage have not been established[30], obesity based on percent body fat was defined as ≥25% and ≥35% for men and women, respectively, to allow for comparability with many other studies that have used similar cut-offs in Asian and Caucasian populations[31-34].

Blood pressure was measured at the right arm in the sitting position using an Omron HEM 7300 oscillometric device (Omron, Matsuka, Japan). Following an overnight fast of 10-12 h confirmed through report of time of last meal, venous blood samples were collected from each participant. Plasma was separated and stored at -80°C. Plasma glucose was assessed via colorimetric analysis at the National Institute of Nutrition, Hyderabad (NIN) within 24 h of sample collection using commercially available GOD-PAP kits (Randox Laboratories, London, UK). The remainder of each sample was transported to the Genetics and Biochemistry Laboratory of the South Asia Network for Chronic Disease (GBL), Public Health Foundation of India, New Delhi, for other biochemical assays. Serum HDL cholesterol was estimated directly by an elimination method and triglycerides by the GPO-PAP method (Roche Diagnostics, Switzerland). Hemoglobin was assessed via the cyanmethemoglobin method using Drabkin's Reagent (Sigma, St. Louis, MO, USA) and cell counter autoanalyzer. The quality of assays was checked with regular external standards (i.e., Randox International Quality Assessment Service) and internal duplicate assays and monitored by the GBL.

Mild anemia among men was defined as a hemoglobin (Hb) concentration of 110-129 g/L and for women 110-119 g/L[35]. Moderate and severe anemia, respectively, among both men and women were defined as Hb concentrations of 80-109 g/L, and < 80 g/L. Men and women with Hb concentrations ≥ 130 g/L, and ≥ 120 g/L, respectively, were considered non-anemic. Participants were classified as having MetS if they had any three of the following five risk factors: 1) abdominal obesity (waist circumference: men, ≥90 cm; women, ≥80 cm); 2) high triglycerides (>150 mg/dL); 3) low HDL cholesterol (men: <40 mg/dL; women: <50 mg/dL); 4) hypertension (≥130/≥85 mmHg); or 5) high fasting glucose (>110 mg/dL). All risk factors and cut-off points were based on current definitions of MetS[36] with the exception that waist circumference cut-offs for defining abdominal obesity were adjusted for Asian Indian populations to reflect the increased cardiovascular risk for these populations at lower waist circumferences[37].

We used two characterizations of the nutritional double burden including the co-occurrence of anemia with 1) overweight according to BMI, and 2) the presence of MetS. In sub-analyses, we also examined the co-occurrence of anemia with obesity according to total body fat percentage from DXA measurements.

Urbanicity was measured by night-time light intensity (NTLI), a data product derived from satellite sensors that capture visible-near infrared emissions from the Earth's surface[38]. Geo-coded village boundaries were applied to 2012 data from the Defense Meteorological Satellite Program – Operational Linescan System (DMSP-OLS), accurate to 1 km resolution, such that NTLI values represent emissions from the village areas only.

Sociodemographic data including the age and level of education of participants, as well as tobacco use, and women's reproductive history were collected using a standardized questionnaire administered by a trained interviewer. An index of household wealth was created using principal components analysis based on household assets. The index included data on housing construction materials, toilet facility, source of lighting, drinking water and cooking fuel, as well as ownership of various durable goods, and agricultural land. Though the raw index score was used in analyses, for purposes of descriptive statistics only, we also examined tertiles of the index score.

Statistical analysis

Statistical analyses were carried out using Stata v. 13.1 (College Station, TX, USA). We calculated sex-specific means and proportions for anemia, overweight, MetS, the co-occurrence of these conditions within an individual, and sociodemographic variables. We conducted two-sided Student's *t*-tests and Pearson's chi-squared tests to assess differences in means and proportions, respectively, between men and women. We calculated the sex-specific expected prevalence of the within-individual double burden as the product of the proportion of individuals with anemia and either overweight or MetS. We examined bivariate associations between sociodemographic characteristics using ANOVA, Pearson's product-moment correlation coefficient (r), and chi-squared tests. In sub-analyses, we examined separate logistic regression models of the association of sociodemographic characteristics with anemia, overweight and the co-occurrence of overweight and anemia, respectively (see **Supplementary Tables 1 and 2**). We also examined these associations with MetS and the co-occurrence of anemia and MetS. However, because the observed prevalence of the co-occurrence of anemia and overweight, and anemia and MetS did not exceed the expected prevalence, we used multinomial logistic regression analyses to simultaneously examine the association of sociodemographic characteristics with each of the four combinations of outcomes. Using the *mlogit* command in Stata, we regressed a four-level outcome variable (i.e., 1) neither anemic nor overweight; 2) anemic; 3) overweight; 4) co-occurrence of anemia and overweight) on sociodemographic characteristics including education, household wealth, and urbanicity. We examined the odds of having the outcome condition, relative to having neither condition, in age-adjusted models and full models that adjusted for all primary sociodemographic variables as well as age, tobacco use, adult stunting, and treatment assignment of individuals in the original HNT trial. These same analyses were carried out for the co-occurrence of anemia and MetS, and in sub-analyses, for the co-occurrence of anemia and obesity based on total body fat percentage from DXA measurements (**Supplementary Table 3**). All variables were identified *a priori* as potential determinants of anemia and cardiometabolic disease risk. Analyses were stratified by sex. We also assessed the associations of sociodemographic variables with the individual component factors of MetS using age-adjusted, simple logistic regression. Standard errors and variance-covariance matrices of the estimators were adjusted for intra-village and intra-household correlations in all models using the robust estimator of variance to allow for intragroup correlation (i.e., the *vce (cluster)* command in Stata using village and household-level fixed effects as the cluster variable). Multicollinearity was assessed in all models as well. Parity and age among women were found to be collinear and therefore parity was not included in final models. However, multicollinearity was not observed among any other covariates in any other models. Associations were considered statistically significant at $P<0.05$.

Ethical approval

Ethical clearance for the APCAPS cohort study was provided by the ethics review committees of the National Institute of Nutrition, the Indian Council of Medical Research, the Public Health Foundation of India, the University of Bristol, and the London School of Hygiene and Tropical Medicine. The heads and governing committees of each of the 29 villages also provided verbal permissions. Written informed consent for inclusion in the study or witnessed thumbprint if illiterate was obtained from each participant prior to enrolment.

Results

There were 6,928 observations from the third wave data set for which anthropometric and hematological data were available. All men and non-pregnant women aged 18 y and older were included in analyses. We excluded 628 participants who were less than 18 y of age and 83 pregnant women. Therefore, our final sample was 6,217 participants from 2,805 unique families. In total, 1,308 participants were index children from the original HNT trial and the remaining participants were their parents (n=2,825), siblings (n=2,075), or step-relatives (n=9).

Men and women constituted 53% and 47% of the sample, respectively (mean age in years (SD): men: 35 (15); women: 36 (12)). More than half of women in the sample were illiterate (55%) compared with approximately only one-quarter of men (26%) (P<0.001) (**Table 1**). These proportions were very nearly reversed with respect to completion of post-primary education (men: 48%; women: 26%). Among the entire sample, 1.9% and 5.5% of individuals had ever had a previous diagnosis of diabetes or hypertension, respectively, or were receiving medical treatment for these conditions.

The prevalence of mild to moderate anemia among women was quadruple the prevalence among men (men: 10%; women: 40%) (P<0.001) (**Table 1**). The prevalence of overweight or obesity based on BMI was also higher among women than men (men: 25%; women: 29%) (P<0.001) as was the prevalence of obesity based on total body fat percentage among the subsample who participated in DXA measurement (men: 13%; women: 26%). The prevalence of MetS was the same for both men and women (15%) (P=0.55) (**Table 1**). There were, however, sex differences across several of the underlying conditions of the syndrome. For example, the prevalence of elevated triglycerides and hypertension was higher among men while a larger proportion of women had low HDL cholesterol levels and abdominal obesity (**Table 1**).

The nutritional double burden was not highly prevalent among men. Approximately 1% of men were both overweight and anemic (1.3%), or anemic and experiencing MetS (1.2%) (**Table 2**). The prevalence of the double burden of overweight and anemia, and MetS and anemia, respectively, was markedly higher among women (overweight: 9%; MetS: 4.5%). The expected prevalence of both double burden characterizations was higher than the observed prevalence (mean difference (range): 0.7 (0, 1.5)) (**Table 2**).

Bivariate associations between sociodemographic characteristics

Household wealth was positively associated with both education and urbanization among both men and women (P<0.001). More highly educated men and women were also more likely to reside in urban areas, however, this association was only observed for individuals with secondary or post-secondary education (P<0.01).

The indicators of overweight and obesity that we examined were highly positively correlated with one another (abdominal obesity and obesity as defined by BMI: r = 0.65, P<0.0001; abdominal obesity and total body fat percentage: r = 0.50, P<0.0001; total body fat percentage and obesity as defined by BMI: r = 0.51, P<0.0001).

Total body fat percentage was not associated with stunting among men (P=0.71). However, stunted women did have a higher total body fat percentage as compared to non-stunted women (P=0.004).

Sociodemographic patterning of anemia and cardiometabolic disease risk

In fully adjusted models for both men and women that examined the odds of being anemic as compared to neither anemic nor overweight, education, household wealth, and urbanicity were not associated with anemia (**Table 3**). Literacy or higher education among men was positively associated with overweight in both age-adjusted and full models (**Table 3**). In fully adjusted models, the odds of being overweight were modestly lower among women with a post-primary education ($P<0.1$). Household wealth showed consistent positive associations with overweight as well as the co-occurrence of overweight and anemia across both sexes. Higher education among men was similarly positively associated with the co-occurrence of overweight and anemia (OR (95% CI): 1.7 (1.1, 2.5)). Yet, the odds of being both anemic and overweight as compared to neither anemic nor overweight was lower among women with a post-primary education as compared to women with no education (OR (95% CI): 0.59 (0.42, 0.82)). These associations, and all others examined, were analogous using multinomial models and adjusted logistic regression models (**Supplementary Tables 1 and 2**).

Higher education was associated with greater odds of MetS among men (OR (95% CI): 1.4 (0.99, 2.0)) (**Table 4**). In fully adjusted models, the odds of having MetS were lower among women with a post-primary education (OR (95% CI): 0.54 (0.29, 0.99)). Household wealth and urbanicity were positively associated with MetS across all models. The co-occurrence of anemia and MetS demonstrated similar sociodemographic patterning as the co-occurrence of overweight and anemia.

In fully adjusted models, age was associated with higher odds of overweight and MetS, respectively, among both men and women (*P*<0.001). The odds of being anemic were higher among women who used tobacco as compared to women who did not use tobacco (*P*<0.05), and the odds of being overweight were lower among men who used tobacco (*P*<0.01). Associations between treatment assignment of individuals in the original HNT trial and being overweight or having anemia among men or women were consistent with random variability (*P*>0.05).

In age-adjusted analyses examining associations between sociodemographic variables and the underlying components of MetS, with few exceptions, household wealth and urbanicity were consistently associated with higher odds of each component condition (**Table 5**). Among men, higher education was also associated with greater odds of each MetS component condition. Among women, a primary school education was associated with greater odds of abdominal obesity (OR (95% CI): 2.23 (1.57, 3.18) and low HDL cholesterol (1.43 (1.03, 1.98)), yet education was not associated with other MetS component conditions, and post-primary education was in fact associated with a lower odds of hypertension among women (OR (95% CI): 0.65 (0.43, 0.99)).

Discussion

We examined the differential extent and determinants of anemia, cardiometabolic disease risk factors, and the co-occurrence of these conditions among adult men and women in an urbanizing region of southern India. Women were four times as likely to be anemic as compared to men, a disparity considerably larger than that observed at the national level across rural India (i.e., anemia among rural men and women nationally: 55% and 75%, respectively) though the overall prevalence of anemia was much lower in this region[39]. Women also showed a higher prevalence of overweight or obesity as compared to men (men: 25%; women: 29%)—a greater difference than that observed in rural areas nationally (i.e., nationally: men: 20%; women: 23%)[40]. Using data on total body fat percentage from DXA measurements, this disparity in the prevalence of obesity between men and women is even greater, with the prevalence of obesity among women double that of men (men: 13%; women: 26%). The prevalence of abdominal obesity among women was also more than double that among men (women: 18%; men: 8%).

Within-sex differences in the prevalence of obesity across the three different indicators assessed were also observed. Though the prevalence of obesity in women based on BMI and waist circumference did not differ greatly (BMI ≥ 25: 16%; waist circumference ≥80 cm: 18%), the prevalence of obesity based on total body fat percentage (≥ 35%) was higher at 26%. Clear cut-offs for defining obesity based on body fat percentage have not been established[30], and therefore, the cut-off for obesity in women based on total body fat percentage may overestimate the prevalence of obesity in women in this population. Within-sex differences for men in the prevalence of obesity using different indicators were overall not as marked as for women (BMI ≥ 25: 13%; total body fat percentage ≥ 25%: 13%; waist circumference ≥90 cm: 8%). Though the different indicators used are attempting to assess the same underlying phenomenon—obesity (i.e., excess body fat)—they are fundamentally different proxies and are certainly imperfect metrics [41]. Importantly, though the prevalence estimates of obesity differed somewhat across indicators, the relationships between the determinants of obesity and the co-occurrence of obesity and anemia were quite consistent across analyses using these different indicators.

Women of childbearing age (15-49 y), who constituted nearly 90% of the women in this sample, are especially susceptible to anemia due to menstruation-related blood loss and the increased nutritional demands of pregnancy and lactation[42]. At the same time, our data indicate that women in this region of India are more at risk of overweight and obesity as compared to men. These findings are aligned with studies from similar developing regions. In China, women had a higher prevalence of both MetS, anemia, and the co-occurrence of the two conditions as compared to men (MetS: 14%, 8.4%; anemia: 32%, 16%; co-occurrence: 4.3%, 1.2%)[43]. Similarly, in Burkina Faso, the prevalence of overweight was higher among women than men (34%, 16%) as was the prevalence of the co-existence of a nutritional deficiency (e.g., iron depletion, anemia, vitamin A deficiency) with a cardiometabolic disease risk factor (e.g., hypertension, hyperglycemia, low HDL cholesterol) (30%, 16%)[44].

Long-term effects of malnutrition early in life may, in part, help to explain the disparity observed in obesity between sexes. Nutritional deficits early in life have been shown to be associated with an increased risk of central obesity and chronic disease in adulthood[45]. This may be particularly true in India where children born with weight deficits to undernourished mothers have comparatively larger deficits in lean mass as compared to fat mass, and therefore may be at greater risk of central obesity in later life[46]. In our sample, 52% of women were stunted as adults compared to 42% of men. Stunting was not associated with adiposity among men, but was positively associated with adiposity among women. Early life stunting then, that is not corrected, may lead to a disproportionately greater risk of adiposity in later life for women as compared to men.

Obesity in India is still largely concentrated among upper socioeconomic groups[19, 47]. Indeed, in this sample, household wealth was consistently associated with greater odds of overweight and MetS among both men and women. Yet, independent of household wealth, higher education was also associated with greater odds of overweight and MetS among men and lower odds among women. There was also a consistent, though statistically non-significant, trend of lower odds of abdominal obesity, high triglycerides, and high glucose among women. There may be several reasons for these contrasting associations. It is possible that collider bias may have been introduced through the conditioning on covariates in fully adjusted models[48]. Yet, it is not clear the extent to which this bias may have been introduced. The odds of women with post-primary education being overweight or having MetS were lower in fully adjusted as compared to age-adjusted models. This difference in the magnitude of the coefficient on post-primary education became apparent when adjusting for household wealth, suggesting that omitting household wealth from the model may lead to confounding bias[49]. Indeed, though correlated, household-level wealth and individual-level educational attainment are distinct constructs and have been shown to have independent influences on health outcomes[50]. These two variables were in fact not collinear in regression models. Higher education among women has been shown to have negative associations with obesity at the same time as household income has demonstrated positive associations[51-53]. Importantly, in age-adjusted models, a primary school education among women was positively correlated with overweight, and some of the component condition of MetS. Therefore, post-primary education among women, and not necessarily any education, may be important for reducing risk of adverse outcomes. While higher education likely has direct health-related benefits independent of wealth[54], women who achieve an education beyond primary school, despite the comparatively high barriers to women receiving an education in India as compared to men[4], may also possess other inherent qualities (e.g., motivation, self-efficacy) or have greater knowledge that predisposes them to making positive choices related to diet, physical activity and health-seeking behavior. These traits, though not measured, may co-vary with education and may be negatively associated with cardiometabolic disease risk factors.

Urbanicity was also positively associated with overweight and MetS. Though the study region has experienced increasing urbanization over the past three decades, it is still predominantly rural. Yet, even low levels of urbanicity, in this semi-rural region, showed a consistent association with overweight and MetS suggesting that the food and activity environments that in part define urban spaces may strongly contribute to cardiometabolic disease risk even in semi-rural areas.

Few sociodemographic factors were associated with anemia. Household wealth, urbanicity, and education were not consistently associated with anemia. The prevalence of anemia in India has been shown to be high across all BMI groups and only marginally higher among thin women as compared to overweight women[55]. Taken together, these findings suggest that economic development efforts may be effective at reducing chronic energy deficiency, but less so at reducing micronutrient deficiencies associated with anemia.

The fact that the observed prevalence of the double burden conditions was not larger than the expected prevalence, suggests that these double burden conditions are not statistically independent of their components. This same finding has been observed for the nutritional double burden of stunted preschool-aged children and overweight mothers within the same household[56]. Though individuals experiencing this double burden may not require unique intervention, the continued high prevalence of anemia in India despite economic development, and the precipitous rise in obesity and associated cardiometabolic disease mean that the convergence of these dual forms of malnutrition will likely continue to increase (one in seven women in this region already experience both conditions) and will require increasing attention from public health policy. Furthermore, iron deficiency, a primary cause of anemia, may in fact be exacerbated by the low-grade, chronic inflammation characteristic of obesity[15] and may contribute to poor glycemic control among both diabetic and non-diabetic patients[57]. Therefore, these component conditions of the double burden may not only co-occur with increasing frequency, but may also interact to yield undesirable outcomes. Though little socioeconomic patterning has been observed previously in association with the individual-level double burden[58], among women in this study, a post-primary education was negatively correlated with both double burden manifestations. For women in particular then, education may be an important policy lever for confronting the double burden.

Though we examined associations in this study among a well-characterized cohort, with data on multiple risk factors of cardiometabolic risk, our study is also subject to the well-known limitations of cross-sectional analyses. We therefore cannot ascribe causal inferences to the observed associations and cannot rule out the possibility that unmeasured confounding bias is present. However, our models adjusted for a comprehensive set of sociodemographic characteristics that were not collinear in models and that we identified *a priori* as potentially important predictors of the nutritional double burden. Thus, we expect that missing variable bias may be limited. Furthermore, we did not include data on the dietary intake or physical activity of respondents as covariates in our models. Though these factors have been shown to be associated with household socioeconomic status and urbanicity, respectively, both of which were included in adjusted models, it is possible that including these data in models could have further limited confounding bias[59, 60]. In addition, the asset-based wealth index that we developed as an indicator of household wealth was not validated in this specific context. However, the index is the same as that used for the National Family Health Surveys (NFHS) of India and follows the same weighted scores to classify the wealth status of populations. Furthermore, using principal components analysis to develop asset-based indices is a common approach to assessing household wealth in LMICs that has been used in many different contexts[50]. Therefore, the use of this index is likely still a robust approach to assessing wealth in this context.

Women in this urbanizing region of southern India bear a larger burden of both anemia and cardiometabolic disease risk and are therefore, more vulnerable to the nutritional double burden as compared to men. The prevalence of both anemia and excessive adiposity among women in this population is substantial and likely reflects the advance of the nutrition transition in India. Though the burden of chronic disease is currently socially segregated in India, as this transition progresses, obesity may increasingly become an affliction of the poor as has been observed in higher income countries. However, the rapid pace of this transition, the particular vulnerability of Asian Indians to the adverse health consequences of overweight, and the increasingly blurred boundary between urban and rural food environments[2], has contributed to an emerging double burden of malnutrition in India as in other LMICs that has rarely been observed in previous development trajectories. The substantial burden of both obesity and anemia among women in this Indian population, and the positive association of household wealth with these conditions suggests that economic growth alone may be insufficient to address these dual manifestations of malnutrition. It is likely that continued investments in women's and girls' education as well as in social support and health services will be needed as the nutrition transition continues to evolve in India. Further research is needed on the biological and social determinants and consequences of this double burden in diverse contexts throughout LMICs to inform public health policies that may address both burdens, especially among women of childbearing age.

Acknowledgements

We thank our dedicated field teams led by Santhi Bogadi and the study participants who made this study possible. P.P., V.G., B.K., G.D.S., Y.B.S., K.V.R., and S.K. contributed to the design of the study; P.P., V.G., B.K., K.V.R., U.K., C.B., A.H., and S.K. contributed to the implementation of the study; A.D.J. analyzed the data and wrote the first draft of the manuscript. All authors contributed to the interpretation of the data, the writing of the manuscript, and have read and approved the final manuscript. A.D.J has primary responsibility for the final content of the manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

Supplementary information

Supplementary information is available at EJCN's website.

References

1. Popkin BM. The nutrition transition: an overview of world patterns of change. Nutr Rev 2004; **62**:S140-3.

2. Kinra S, Bowen LJ, Lyngdoh T, Prabhakaran D, Reddy KS, Ramakrishnan L, *et al.* Sociodemographic patterning of non-communicable disease risk factors in rural India: a cross sectional study. *BMJ* 2010; **341**:c4974.

3. Caballero B. A nutrition paradox--underweight and obesity in developing countries. *N Engl J Med* 2005; **352**:1514-6.

4. International Institute for Population Sciences. *National Family Health Survey (NFHS-3) India 2005-2006, Volume 1*. Mumbai: International Institute for Population Sciences, 2007.

5. Prentice AM. The emerging epidemic of obesity in developing countries. International. *Journal of Epidemiology* 2006; **35**:93-99.

6. Prasad DS, Kabir Z, Dash AK, Das BC. Prevalence and risk factors for metabolic syndrome in Asian Indians: A community study from urban Eastern India. *J Cardiovasc Dis Res* 2012; **3**:204-11.

7. Sawant A, Mankeshwar R, Shah S, Raghavan R, Dhongde G, Raje H, *et al*. Prevalence of Metabolic Syndrome in Urban India. *Cholesterol* 2011:10.1155/2011/920983.

8. Kanjilal S, Shanker J, Rao VS, Khadrinarasimhaih NB, Mukherjee M, Iyengar S, *et al*. Prevalence and component analysis of metabolic syndrome: an Indian atherosclerosis research study perspective. *Vasc Health Risk Manag* 2008; **4**:189-97.

9. Kamble P, Deshmukh PR, Garg N. Metabolic syndrome in adult population of rural Wardha, central India. *Indian J Med Res* 2010; **132**:701-705.

10. Eapen D, Kalra GL, Merchant N, Arora A, Khan BV. Metabolic syndrome and cardiovascular disease in South Asians. *Vascular Health and Risk Management* 2009; **5**:731-743.

11. Garcia OP, Long KZ, Rosado JL. Impact of micronutrient deficiencies on obesity. *Nutrition* 2009; **67**:559-572.

12. Kraemer K, Zimmermann MB. *Nutritional Anemia* (Kraemer K and Zimmermann MB, eds). Switzerland: Sight and Life Press, 2007.

13. Cordain L, Eaton SB, Sebastian A, Mann N, Lindeberg S, Watkins BA, *et al.* Origins and evolution of the Western diet: health implications for the 21st century. *American Journal of Clinical Nutrition* 2005; **81**: 341-354.

14. Zimmermann MB, Zeder C, Muthayya S, Winichagoon P, Chaouki N, Aeberli I, *et al.* Adiposity in women and children from transition countries predicts decreased iron absorption, iron deficiency and a reduced response to iron fortification. *Int J Obes* 2008; **32**: 1098-104.

15. Tussing-Humphreys L, Pusatcioglu C, Nemeth E, Braunschweig C. Rethinking iron regulation and assessment in iron deficiency, anemia of chronic disease, and obesity: introducing hepcidin. *J Acad Nutr Diet* 2012; **112**:391-400.

16. Yanoff LB, Menzie CM, Denkinger B, Sebring NG, McHugh T, Remaley AT, *et al*. Inflammation and iron deficiency in the hypoferremia of obesity. *Int J Obes* 2007; **31**(9): 1412-9.

17. World Health Organization. *Worldwide prevalence of anaemia, 1993–2005*. Geneva, Switzerland: World Health Organization, 2008.

18. Subramanian SV, Smith GD. Patterns, distribution, and determinants of under- and overnutrition: a population-based study of women in India. *Am J Clin Nutr* 2006; **84**: 633-40.

19. Subramanian SV, Perkins JM, Khan KT. Do burdens of underweight and overweight coexist among lower socioeconomic groups in India? *Am J Clin Nutr* 2009; **90**:369-76.

20. Griffiths PL, Bentley ME. The Nutrition Transition Is Underway in India. *Journal of Nutrition* 2001; **131**:2692-2700.

21. Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. *Nutr Rev* 2012; **70**:3-21.

22. Kinra S, Rameshwar SKV, Ghafoorunissa, Mendu VV, Ravikumar R, Mohan V, *et al.* Effect of integration of supplemental nutrition with public health programmes in pregnancy and early childhood on cardiovascular risk in rural Indian adolescents: long term follow-up of Hyderabad nutrition trial. *BMJ* 2008; **337**:a605.

23. Kinra S, Radha Krishna K, Kuper H, Rameshwar SK, Prabhakaran P, Gupta V, *et al.* Cohort Profile: Andhra Pradesh Children and Parents Study (APCAPS). *Int J Epidemiol* 2013; **43**:1417-24.

24. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, *et al.* Consensus statement for diagnosis of obesity, abdominal obesity and the

metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. *J Assoc Physicians India* 2009; **57**:163-70.

25. Snehalatha C, Viswanathan V, Ramachandran A. Cutoff values for normal anthropometric variables in asian Indian adults. *Diabetes Care* 2003; **26**: 1380-4.

26. Deurenberg P, Yap M, Staveren W. Body mass index and percent body fat: a meta analysis among different ethnic groups. *Intl J Obes* 1998; **22**: 1164-71.

27. Gregory CO, Corvalán C, Ramirez-Zea M, Martorell R, Stein AD. Detection of cardio-metabolic risk by BMI and waist circumference among a population of Guatemalan adults. *Public Health Nutrition* 2008; **11**(10): 1037-1045.

28. Coly AN, Milet J, Diallo A, Ndiaye T, Benefice E, Simondon F, *et al.* Preschool stunting, adolescent migration, catch-up growth, and adult height in young senegalese men and women of rural origin. *J Nutr* 2006; **136**(9): 2412-20.

29. National Center for Health Statistics. *CDC Growth Charts: United States*. Atlanta, GA: National Center for Health Statistics, 2000. Available from: http://www.cdc.gov/growthcharts/.

30. Ho-Pham LT, Lai TQ, Nguyen MTT, Nguyen TV. Relationship between Body Mass Index and Percent Body Fat in Vietnamese: Implications for the Diagnosis of Obesity. *PLoS ONE* 2015; **10**(5): e0127198.

31. Romero-Corral A, Somers VK, Sierra-Johnson J, Thomas RJ, Collazo-Clavell ML, Korinek J, *et al.* Accuracy of body mass index in diagnosing obesity in the adult general population. *Int J Obes* 2008; **32**(6): 959-66.

32. Deurenberg-Yap M, Chew SK, Deurenberg P. Elevated body fat percentage and cardiovascular risks at low body mass index levels among Singaporean Chinese, Malays and Indians. *Obes Rev* 2002; **3**(3): 209-15.

33. Deurenberg P, Weststrate JA, Seidell JC. Body mass index as a measure of body fatness: age- and sex-specific prediction formulas. *Br J Nutr* 1991; **65**(2): 105-14.

34. Adams KM, Lindell KC, Kohlmeier M, Zeisel SH. Status of nutrition education in medical schools. *American Journal of Clincal Nutrition* 2006; **83**(4): 941S-944S.

35. World Health Organization. *Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity*. Geneva, Switzerland: World Health Organization, 2011.

36. National Cholesterol Education Program. *Adult Treatment Panel III Guidelines*. Washington, DC: National Heart, Lung, and Blood Institute, 2001.

37. Misra A, Vikram NK, Gupta R, Pandey RM, Wasir JS, Gupta VP, *et al.* Waist circumference cutoff points and action levels for Asian Indians for identification of abdominal obesity. *Int J Obes* 2006; **30**:106-11.

38. National Oceanic and Atmospheric Administration. *NOAA National Geophysical Data Center Earth Observation Group.* 2014. Accessed May 22, 2014; Available from: http://ngdc.noaa.gov/eog/.

39. National Nutrition Monitoring Bureau. *Diet & Nutritional Status of Population and Prevalence of Hypertension among Adults in Rural Areas*. Hyderabad, India: National Institute of Nutrition, 2006.

40. National Nutrition Monitoring Bureau. *Diet and Nutritional Status of Rural Population, Prevalance of Hypertension & Diabetes among Adults and Infant & Young Child Feeding Practices: Report of Third Repeat Survey*. Hyderabad, India: National Institute of Nutrition, 2012.

41. Ahima RS, Lazar MA. The Health Risk of Obesity—Better Metrics Imperative. *Science* 2013; **341**(6148): 856-858.

42. World Health Organization. *Daily iron and folic acid supplementation in pregnant women*. Geneva, Switzerland: World Health Organization, 2012.

43. Shi Z, Hu X, Yuan B, Hu G, Pan X, Holmboe-Ottesen G. Coexistence of anaemia and the metabolic syndrome in adults in Jiangsu, China. *Asia Pac J Clin Nutr* 2008; **17**:505-13.

44. Zeba AN, Delisle HF, Renier G, Savadogo B, Baya B. The double burden of malnutrition and cardiometabolic risk widens the gender and socio-economic health gap: a study among adults in Burkina Faso (West Africa). *Public Health Nutr* 2012; **15**:2210-9.

45. Ravelli AC, van der Meulen JH, Osmond C, Barker DJ, Bleker OP. Obesity at the age of 50 y in men and women exposed to famine prenatally. *Am J Clin Nutr* 1999; **70**: 811-6.

46. Yajnik CS, Fall CH, Coyaji KJ, Hirve SS, Rao S, Barker DJ, *et al.* Neonatal anthropometry: the thin-fat Indian baby. The Pune Maternal Nutrition Study. *Int J Obes Relat Metab Disord* 2003: **27**:173-80.

47. Subramanian SV, Corsi DJ, Subramanyam MA, Smith GD. Jumping the gun: the problematic discourse on socioeconomic status and cardiovascular health in India. *Int J Epidemiol* 2013; **42**:1410-26.

48. Cole SR, Platt RW, Schisterman EF, Chu H, Westreich D, Richardson D, *et al.* Illustrating bias due to conditioning on a collider. *Int J Epidemiol* 2010; **39**:417-20.

49. Hosmer DW, Lemeshow S. *Applied Logistic Regression*. New York, NY: Wiley, 2010.

50. Rutstein SO, Johnson K. *The DHS Wealth Index*. Calverton, MD: ORC Macro, 2004.

51. Winkleby MA, Jatulis DE, Frank E, Fortmann SP*.* Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. *American Journal of Public Health* 1992; **82**:816-820.

52. Monteiro CA, Conde WL, Popkin BM. Independent Effects of Income and Education on the Risk of Obesity in the Brazilian Adult Population. *J Nutr* 2001; **131**:881S-886S.

53. Herd P, Goesling B, House JS. Socioeconomic Position and Health: The Differential Effects of Education versus Income on the Onset versus Progression of Health Problems. *Journal of Health and Social Behavior* 2007; **48**:223-238.

54. Baker DP, Leon J, Smith Greenaway EG, Collins J, Movit M*.* The Education Effect on Population Health: A Reassessment. *Population and Development Review* 2011; **37**:307-332.

55. Bentley ME, Griffiths PL. The burden of anemia among women in India. *Eur J Clin Nutr* 2003; **57**:52-60.

56. Dieffenbach S, Stein AD. Stunted child/overweight mother pairs represent a statistical artifact, not a distinct entity. *J Nutr* 2012; **142**:771-3.

57. Coban E, Ozdogan M, Timuragaoglu A. Effect of iron deficiency anemia on the levels of hemoglobin A1c in nondiabetic patients. *Acta Haematol* 2004; **112**:126-8.

58. Gartner A, El Ati J, Traissac P, Bour A, Berger J, Landais E, *et al.* A double burden of overall or central adiposity and anemia or iron deficiency is prevalent but with little socioeconomic patterning among Moroccan and Tunisian urban women. *J Nutr* 2014; **144**:87-97.

59. Yadav K, Krishnan A. Changing patterns of diet, physical activity and obesity among urban, rural and slum populations in north India. *Obesity Reviews* 2008; **9**(5): 400-408.

60. Thorne-Lyman AL, Valpiani N, Sun K, Semba RD, Klotz CL, Kraemer K, *et al.* Household dietary diversity and food expenditures are closely linked in rural

Bangladesh, increasing the risk of malnutrition due to the financial crisis. *J Nutr* 2010; **140**(1): 182S-8S.