RESEARCH PAPER

Variability of Thinness and its Relation to Cardio-metabolic Risk Factors using Four Body Mass Index References in School-children from Delhi, India

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Objectives: To compare: (*i*) prevalences of thinness in school-children by four body mass index references in common use *viz*., Centre for Disease Control (CDC); Cole; Indian Academy of Pediatrics (IAP); World Health Organization (WHO); and (*ii*) relationship of thinness with absence of cardio-metabolic risk factors in these BMI references.

Design: Cross-sectional.

Setting: Schools in Delhi.

Participants: Anthropometry and blood pressure were measured in 16,245 school children aged 5 to 18 years. Fasting lipids and blood sugar were estimated in 2796 subjects.

Outcome measures: Age and sex-specific prevalences of thinness and predictive ability of reference cut-off for detecting any cardio-metabolic risk factor were compared.

Results: Prevalence of thinness varied with the reference employed; more so for boys. Overall prevalence of thinness was least with IAP reference and highest with CDC cut-offs (6.6% to 16.9% in boys, 6.5% to 10.3% in girls). Children identified as thin by any reference had comparable, significantly lower risks (OR 0.59 to 0.73) of associated cardio-metabolic aberrations. In subjects with any cardio-metabolic or blood pressure aberration, the prevalence of thinness was highest with CDC and least with IAP definition.

Conclusion: Prevalence of thinness varies considerably with the reference employed. Thin children, identified by any reference, have a lower risk of associated cardio-metabolic aberrations; however, thinness is a poor diagnostic test for this purpose. In populations undergoing nutrition transition, there is a need to link cardio-metabolic risk factors with recommended anthropometric criteria to define undernutrition.

Keywords: *Body mass index, Cholesterol, Glucose, Hypertension, Thinness, Triglyceride.*

Published online: June 5, 2013; PII: S097475591200871

Adults below a body mass index (BMI) of 18.5 kg/m^2 are classified as thin or underweight [1,2]. This concept has been extrapolated to adolescents and children to develop gender and age-specific BMI cut-offs to assess prevalence of thinness [2,3] in various settings, Centre for Disease Control (CDC) and World Health Organization (WHO) BMI charts are also available for this purpose [4,5]. The availability of multiple cut-offs based on different BMI references poses a challenge both for clinical practice and for quantification of public health burden. Considerable variations in prevalences of obesity (9.3% to 21% in boys, 4.1% to 35% in girls) and metabolic syndrome abnormalities in anthropometrically obese children are documented with use of different BMI references in various settings [6-11]. Considerable variations may likewise occur for thinness, even in low and middle income countries (LMICs).

The National Family Health Survey (NFHS-3) data from India has documented a high prevalence of undernutrition in children younger than five years using WHO multi-country growth reference [12,13]. However, there is paucity of similar nationally representative data in older children and adolescents. The estimated burden of thinness (undernutrition) from future, relevant data sets may be substantially influenced by the choice of growth standard. It is therefore important to understand

and quantify the variations in prevalences of thinness, if any with the commonly employed, international and national, BMI references in older children and adolescents.

In LMICs, anthropometrically undernourished children are often prescribed food supplementation to improve body size. However, cardio-metabolic risk factors (proxy for overnutrition) can also theoretically occur in a proportion of anthropometrically undernourished children, especially in settings of rapid nutrition transition. In the short-term, food supplementation may worsen cardio-metabolic risk factors in such individuals. In the long term, if this intervention leads to adult overweight or obesity, the propensity to develop chronic diseases and hypertension will increase [14-16]. It is therefore also important to determine if thinness predicts absence of cardio-metabolic risk factors and whether this relationship alters with different BMI references.

This study was therefore designed to compare: (*i*) prevalences of thinness in school-children by four BMI references in common use, namely, Cole, *et al*. [2], WHO [4], CDC [5] and Indian Academy of Pediatrics (IAP) [17]; and (*ii*) relationship of thinness with absence of cardio-metabolic risk factors in these BMI references.

METHODS

This cross-sectional study was conducted between January 2005 and March 2007. All the public and private schools in National Capital Territory of Delhi were enlisted and stratified into low (LIG), middle (MIG) and high (HIG) income groups on the basis of fees charged. Government and Municipal Corporation of Delhi schools were considered as LIG, Kendriya Vidhalayas as MIG and private schools charging monthly tuition fees above Rs.1000 as HIG. Probability proportionate to size (PPS) sampling methodology was utilized for selection of 90 schools. In each of the socio-economic group, 30 clusters were selected. We evaluated 180 ± 10 subjects, between 5 and 18 years of age, from each cluster. Written informed consent was taken from the school authorities and parents. Institutional ethics approval was granted by the All India Institute of Medical Sciences, New Delhi.

Weight and height were recorded using standard methodology [18]. Weight was recorded on SECA electronic weighing scale to the nearest 100g. Height was recorded on anthropometric height board to the nearest 0.1cm. Three readings of height and weight were taken, and the mean of the last two readings was recorded. Systolic and diastolic blood pressures after a period of 10 minutes rest were measured in sitting position with an appropriate sized cuff on a mercury sphygmomanometer. Three readings were taken, and their mean was considered as the individual's blood pressure. All these measurements were recorded by trained nutritionists.

In consenting subjects, 5mL of fasting blood sample was transported to laboratory for estimating serum total cholesterol, triglyceride, high density lipoprotein (HDL) and sugar. For quality assurance, three levels of internal controls were run with each batch of twenty samples. The intra-assay and inter-assay variation was less than 2% and 3%, for cholesterol and triglyceride levels, respectively; and less than 2.5% and 3.5% for HDL cholesterol and sugar, respectively. Estimation of total serum cholesterol was done by CHOD-PAP (cholesterol oxidase/p-aminophenazone) method and triglycerides by GPO-PAP (glycerolphosphate oxidase–peroxidase amino-phenazone) method [19,20]. High-density lipoprotein cholesterol (HDL) was estimated by the precipitation method using phosphotungstate/magnesium precipitation of apolipoprotein B containing lipoproteins followed by the estimation of cholesterol in the supernatant by enzymatic method. Low density lipoprotein (LDL) was calculated using Friedewald formula [21]. Fasting glucose was estimated using the standard glucose oxidase method. Estimations of all these biochemical parameters were available in 2796 children (LIG – 626, MIG – 962, HIG – 1208).

Pre-hypertension was defined as systolic and diastolic blood pressure between 90th to 95th percentile (z-scores 1.282-1.645), and hypertension >95th percentile (z-score >1.645), using the sex and height adjusted Centre for Disease Control (CDC, 2000) standards for the American children [22]. Dyslipidemia (either hypertriglyceredemia ≥200 mg/dL, or low HDL cholesterol <40 mg/dL, or high LDL cholesterol ≥100 mg/dL or hypercholesterolemia ≥170 mg/dL) was defined according to American Heart Association (AHA) guidelines, endorsed by the American Academy of Pediatrics [23]. At these cut-offs dietary and/or life style interventions are suggested [23,24]. Impaired glucose tolerance was defined as fasting plasma glucose levels ≥100 mg/dL [25]. The AHA cut-off values for fasting plasma glucose and HDL cholesterol corresponded with the International Diabetes Federation (IDF) definition of metabolic syndrome in children and adolescents [26]. However, the cut-off for triglyceride was lower (≥1.7 mmol/l or ≥150 mg/dL) with IDF criteria [26].

Statistics: Statistical analysis was done using SPSS version 13.0 (SPSS Inc, Chicago, Illinois, USA). We had the recorded age to the exact day, which was grouped into 0.1 yearly intervals. However, the cut-off values for BMI

references were depicted at half-monthly [5], monthly [4], half-yearly [2] and yearly [17] intervals. In order to obtain precise numerical cut-offs at 0.1 yearly intervals, smoothing was required for the intervening time points. This was achieved by polynomial curve regression [27] using the stated cut-offs at different ages [2,4,5,17] as anchors, so that these values remained virtually identical after smoothing. The degree of polynomial used was based on the best fit and varied for the four references (seventh degree for the Cole, CDC and WHO references and fourth degree for IAP reference).

The gender specific age ranges for comparison were identified according to the ages where the smoothed curves of BMI from the four references crossed or touched each other (***Fig.* 1**). Age and sex-specific prevalences of thinness, defined as per the cut-offs recommended by the four BMI references [2,4,5,17], were compared. The cut-offs used were below -2 SD (Z score) for WHO [4] and CDC [5] references; below age and gender specific extrapolation of BMI of 17 at 18 years, which correspond to a mean Z score of -2, for Cole *et al*. [2] reference; and below 5th percentile for IAP reference [17].

Sex and height adjusted Z-scores for systolic and diastolic blood pressure of children were calculated using separate equations as recommended [22]. We also compared the odds ratio, sensitivity, specificity, predictive values and likelihood ratios for detecting any cardio-metabolic risk factor in children identified as thin using various BMI references.

RESULTS

Subjects consenting for blood-letting were more often females and had significantly greater age, socio-economic class, height-for-age (0.2 Z-score), weight-for-age (0.8 Z-score) and BMI-for-age (0.5 Z-score) (P<0.001 for all variables). The age, gender and socio-economic class adjusted Odds Ratio (95% CI) for being sampled per unit increase in BMI-for-age Z score was 1.10 (1.09, 1.12).

Descriptive characteristics of the subjects are summarized in ***Table* I.** Overall prevalence of thinness varied between 6.6% and 16.9% for boys, and 6.5% and 10.3% for girls using IAP and CDC references, respectively **(*Tables* II** and **III).** The differences were more pronounced for boys as compared to girls. Prevalence with IAP reference was substantially lower than CDC reference for boys across all the age ranges (least for the age range 14.6 to 18.0 years) **(*Table* II).** Thinness prevalence in boys using the CDC and Cole

TABLE I DESCRIPTIVE CHARACTERISTICS OF THE STUDY POPULATION

Income group (Number)	*Mean (SD) age (yrs)*	*Mean BMI (kg/m^2) (SD)[range]*	*Sex*	
			Male	*Female*
LIG (5031)	12.1 (3.5)	16.37 (2.7) [11.2 – 32.8]	2378	2653
MIG (5119)	11.6 (3.3)	16.96 (3.1) [11.2 – 36.7]	2736	2383
HIG (6095)	11.5 (3.1)	18.71 (4.5) [11.0 – 39.3]	3199	2896
Total 16245	11.7 (3.3)	17.44 (3.7) [11.0 – 39.3]	8313	7932

BMI – Body mass index; HIG – High income group; LIG – Low income group; MIG – Middle income group.

TABLE II PREVALENCE OF THINNESS IN BOYS ACCORDING TO FOUR BMI REFERENCES

Reference[a]	*Years*												
	5.0 - 6.5		*Ref*	*6.6 - 9.5*		*9.6 -12.0*		*12.1 -14.5*		*14.6 - 18.0*		*Ref*	*5.0-18.0*	
	n	*%*		*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*		*n*	*%*
CDC	83	18.2	CDC	203	11.0	233	13.4	423	19.3	460	22.0	CDC	1402	16.9
Cole	49	10.7	WHO	154	8.4	211	12.2	413	18.8	423	20.3	WHO	1237	14.9
WHO	36	7.9	Cole	111	6.0	127	7.3	281	12.8	301	14.4	Cole	869	10.5
IAP	20	4.4	IAP	80	4.3	53	3.1	175	8.0	217	10.4	IAP	545	6.6
All[b]	456			1844		1733		2193		2087			8313	

[a] *The references in each age interval are ordered according to the cut-off value in descending order;* [b] *total number of subjects in the age range.*

TABLE III PREVALENCE OF THINNESS IN GIRLS ACCORDING TO FOUR BMI REFERENCES

Years																													
5.0-9.3			9.4-11.1			11.2-12.3			12.4-14.1			14.2-15.0			15.1-15.6			15.7-15.8			15.9-16.9			17.0-18.0			5.0-18.0		
Ref [a]	n	%	Ref	n	%	Ref	n	%	Ref	n	%	Ref	n	%	Ref	n	%	Ref	n	%	Ref	n	%	Ref	n	%	Ref	n	%
CDC	232	9.7	CDC	159	12.0	WHO	94	11.5	WHO	154	11.4	Cole	65	11.0	Cole	39	10.1	Cole	20	16.0	Cole	63	10.7	Cole	50	14.5	CDC	820	10.3
Cole	160	6.7	WHO	134	10.1	CDC	85	10.4	Cole	146	10.8	WHO	62	10.5	WHO	36	9.4	IAP	15	12.0	IAP	53	9.0	CDC	49	14.2	Cole	749	9.4
WHO	127	5.3	Cole	128	9.7	Cole	78	9.5	CDC	135	10.0	CDC	59	9.9	IAP	35	9.1	WHO	14	11.2	CDC	53	9.0	IAP	45	13.1	WHO	712	9.0
IAP	64	2.7	IAP	77	5.8	IAP	54	6.6	IAP	115	8.5	IAP	57	9.6	CDC	34	8.8	CDC	14	11.2	WHO	49	8.3	WHO	42	12.2	IAP	515	6.5
All [b]	2401		All	1324		All	819		All	1352		All	593		All	385		All	125		All	589		All	344			7932	

[a] The references in each age interval are ordered according to the cut-off value in descending order.[b] total number of subjects in the age range.

TABLE V PREVALENCE OF THINNESS ACCORDING TO FOUR DEFINITIONS IN CHILDREN WITH PRE-HYPERTENSION, Hypertension or any Cardio-metabolic Aberration

Boys				Girls			
Definition	Prehypertension (1429 of 8313)	Hypertension (2745 of 8313)	Any cardio-metabolic aberration (906 out of 1320)	Definition	Prehypertension (1310 of 7932)	Hypertension (2875 of 7932)	Any cardio-metabolic aberration (967 out of 1476)
	Thinness prev (%) (n of 1429)	Thinness prev(%) (n of 2745)	Thinness prev (%) (n of 906)		Thinness prev (%) (n of 1310)	Thinness prev(%) (n of 2875)	Thinness prev (%) (n of 967)
CDC	15.9 (227)	10.1 (276)	11.8 (107)	CDC	10.8 (141)	6.9 (198)	7.5 (73)
WHO	13.7 (196)	8.2 (225)	11.0 (100)	Cole	8.6 (112)	6.0 (172)	7.4 (72)
Cole	10.2 (146)	5.7 (156)	6.7 (61)	WHO	8.1 (106)	5.6 (161)	7.9 (76)
IAP	6.4 (92)	3.4 (94)	4.0 (36)	IAP	5.9 (77)	3.5 (101)	5.6 (54)

Prev – Prevalence

Any cardio-metabolic aberration was defined as presence of one or more of the following in an individual subject: fasting levels of blood glucose ≥100 mg/dL or total cholesterol ≥170 mg/dl or LDL cholesterol ≥100 mg/dl or HDL cholesterol <40 mg/dL or serum triglyceride ≥200 mg/dL.

TABLE IV COMPARISON OF FOUR THINNESS CUT-OFFS FOR DIAGNOSING ANY CARDIO-METABOLIC ABERRATION

Thinness cut-off	*Odds ratio (95% CI; P value*	*Sensitivity*	*Specificity*	*Positive predictive value*	*Negative predictive value*	*Positive likelihood ratio*	*Negative likelihood ratio*
CDC	0.73 (0.57, 0.93); 0.011	0.10	0.87	0.60	0.32	0.75	1.04
WHO	0.73 (0.56, 0.93); 0.012	0.09	0.88	0.60	0.32	0.75	1.03
Cole	0.62 (0.48, 0.81); 0.001	0.07	0.89	0.57	0.32	0.65	1.04
IAP	0.59 (0.43, 0.81); 0.001	0.05	0.92	0.55	0.32	0.61	1.03

Any cardio-metabolic aberration was defined as presence of one or more of the following in an individual subject: fasting levels of blood glucose ≥100 mg/dl or total cholesterol ≥170 mg/dl or LDL cholesterol ≥100 mg/dl or HDL cholesterol <40 mg/dl or serum triglyceride ≥200 mg/dl. Odds Ratios were computed by logistic regression analysis and pertain to comparison of thin with non-thin subjects.

references was 18.2% and 10.7%, respectively compared to 7.9% and 4.4% using WHO and IAP references for the age range of 5.0 to 6.5 years **(*Table* II)**. After this age range, prevalence with WHO reference was lower than CDC reference but higher than Cole, *et al*. [2] reference. Prevalence by Cole, *et al*. [2] reference was closer to IAP reference in boys above 6.5 years.

Crossing over of references was more frequent in girls. In girls, maximum variation was seen in youngest age range (5.0-9.3 years). Prevalence with IAP reference was consistently lower compared to other references till the age of 15 years, after which there were no substantial differences between the references. The WHO cut-off estimated lower prevalence in girls after the age of 15.6 years; whereas, CDC cut-off documented lower prevalence after the age of 12.3 years **(*Table* III).**

Children identified as thin by any reference had a significantly lower risk of associated cardio-metabolic risk factors (***Table* IV**); IAP cut-off had the least odds ratio (0.59) but this was not significantly different from the other three references (overlapping confidence intervals). Among children with pre-hypertension, hypertension or any cardio-metabolic aberration, the prevalence of thinness was highest with CDC and least with IAP definition (***Table* V***; P*<0.01). These differences were greater in boys (2.5 to 3 fold) than in girls (1.3 to 2 fold). In boys the thinness prevalence was greater with WHO in comparison to Cole reference, but the converse was true for girls.

DISCUSSION

The prevalence of thinness varied with the reference employed, especially in boys. In comparison to IAP reference, CDC reference overestimated thinness maximally (2-4 fold in boys and up to 3.5 fold in girls). This overestimation was lower with WHO and Cole references. Children identified as thin by any reference had comparable, significantly lower risks of associated cardio-metabolic aberrations. However, in subjects with any cardio-metabolic or blood pressure aberration, the prevalence of thinness was highest with CDC and least with IAP definition.

We have evaluated a large sample of urban school children from different socio-economic strata in a developing country undergoing nutrition transition [13]. Simultaneous differences in the prevalences of anthropometric thinness and cardio-metabolic aberrations warranting interventions [23-26] were quantified. Serum biochemistry was performed in an international quality controlled laboratory.

The following limitations merit consideration: (*i*) We could not adjust for the influence of pubertal growth spurts on BMI as sexual maturity staging was not done. However, this has little relevance as the four evaluated references do not recommend such adjustment for quantifying thinness; (*ii*) In comparison to other criteria, IAP reference [17] had an uncharacteristic shape for boys, especially above 16 years (***Fig*. 1**). This is not due to our smoothing for intervening age-periods but probably reflects weaknesses in original IAP reference – small sample sizes at these ages and not using the recommended LMS method for smoothing. Nevertheless, this has no implications for our stated objectives, because thinness will be categorized according to the depicted cut-offs; (*iii*) Blood sampled participants had significant differences from others including a higher BMI. This has implications for determining overall prevalence of cardio-metabolic risk factors but not for evaluating their relationship with thinness; (*iv*) The high prevalence of pre-hypertension and hypertension needs cautious interpretation. We used CDC percentiles for defining height adjusted pre-hypertension and hypertension rather than an Indian reference to maintain uniformity with other biochemical cut-offs. In comparison to unadjusted

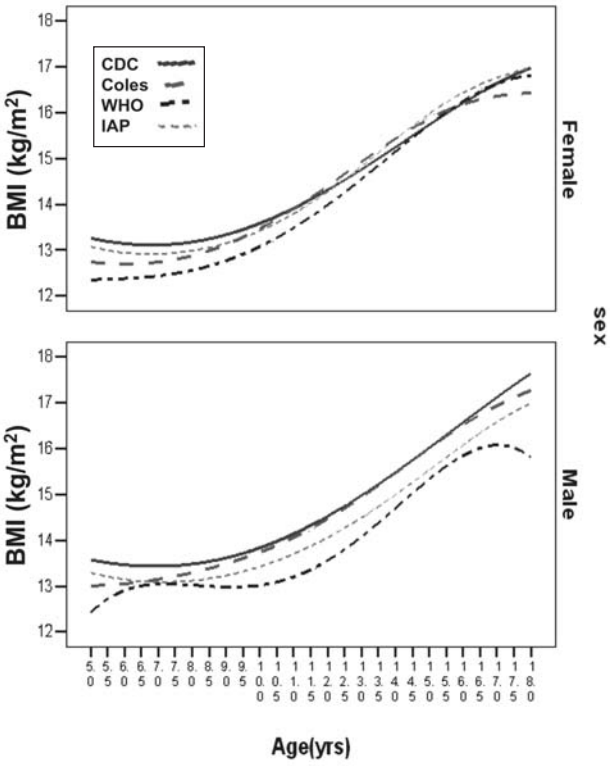

FIG.1 *Comparison of smoothed curves for body mass index limits for defining thinness.*

estimates as in many earlier studies, height adjustment lowers the reference BP thereby inflating the pre-hypertension and hypertension prevalence in shorter populations as in New Delhi (mean height SD score -0.73). We also acknowledge the inherent challenges of blood pressure measurements in children [28]. Blood pressure was recorded during one visit only, which may not reflect sustained hypertension. Among 15-16 year old students from Dallas, USA with elevated BP (≥95th percentile) at initial examination, only 17% had sustained elevated BP over 2 subsequent visits in the same year [29]. Other studies also indicate that the majority of children with elevated BP at a given visit have normal BP at subsequent visits a few weeks later, notably because of regression to the mean and habituation to the measurement procedure [28]. It would thus have been ideal for us to perform two repeat BP measurements; however, paucity of resources precluded this possibility. A high prevalence of systolic or diastolic incident hypertension in children (17.3% in overweight *vs.* 10.1% in others) has been shown in a study on a mixed rural and urban Southern Indian population [30]. Thus the overestimation of blood pressure from a single visit in our data from urban area may not be substantial; and (*v*). A larger sample size would have provided greater power to detect the observed differences in predictive abilities of the references for identifying absence of any cardio-metabolic aberration.

We are unaware of any similar studies comparing the prevalences of cardio-metabolic aberrations in thin children. However, anthropometric and metabolic discordance has been documented in "metabolically obese normal weight" children in a nationally representative sample from Iran [31]. Several studies have documented variations in prevalences of obesity and metabolic syndrome in children and adolescents with use of different references [6-11]. In younger children, overestimation of prevalence of undernutrition with CDC reference has been documented in both developing and developed countries [32-35]. We used cut-off criteria for which nutritional and/or lifestyle interventions are suggested by the AHA [22-25]. The use of IDF definition [26] increased the prevalence of hyper-triglyceridemia from 2.1% to 10.5% without much difference for any cardio-metabolic aberration (67% *vs.* 68%).

From a clinician's perspective, labeling of an individual child as "thin" leads to further diagnostic and therapeutic actions. Absence of data comparing the appropriateness of the management interventions with various cut-offs leads to uncertainty on the utility of one BMI reference over other. Routine recording of blood pressure after the age of three years is recommended in developed country settings to counter obesity related hypertension [24]. It may be a good practice for pediatricians in India to replicate this guideline irrespective of BMI status. Similarly, there may be a case for evaluating the metabolic profile in "at risk" thin children as identified by high blood pressure or a parental history of premature coronary artery disease, hypertension, diabetes mellitus or dyslipidemia. Future research on the utility of these recommendations is required.

In a public health setting, two-to four-fold relative variations in prevalences of thinness have socio-political implications for ranking the development status and progress of nations. Unlike the WHO growth references for under-five children that are conceptualized on prescriptive practices, these evaluated BMI cut-offs are based on statistical charts, which have not been linked to important biological or functional consequences [36,37]. The usual public health and clinical response in thin children is to recommend food supplementation [38,39], which has the potential to worsen cardio-metabolic risk factors including blood pressure. Children identified as thin by any reference had a significantly lower risk of cardio-metabolic aberration (positive likelihood ratios of 0.61 to 0.75 for detecting cardio-metabolic aberration).

Opinions will vary on the usefulness of these predictions. However, according to conventional guidelines [40], such likelihood ratios of <0.2 are generally considered important clinically while values >0.5 are labeled worthless.

Biomarkers can be considered as more proximate reflectors of recent nutritional balance; thus cardio-metabolic aberrations reflect metabolic overnutrition, even in anthropometrically thin ("undernourished") subjects. In this context, from a public health perspective, national reference has the advantage of detecting the least prevalence of thinness in metabolically overnourished individuals. However, further research is needed to validate these findings in different settings.

In conclusion, prevalences of thinness in school-children vary considerably with the reference employed, especially in boys. Thin children, identified by any reference, have a lower risk of associated cardio-metabolic aberrations; however, thinness is a poor diagnostic test for this purpose. In populations undergoing nutrition transition, there is a need to link cardio-metabolic risk factors with recommended anthropometric criteria to define undernutrition.

Acknowledgements: We thank Lieutenant Colonel Dr. Rajat Prakash for training nutritionists, Supreet Kaur (SK), Lakshmi Labani (LL) and Shikha Shukla (SS) for anthropometric and blood pressure measurements.

Contributors: HPSS, UK and PG: conceived the study, analysis and co-drafted the manuscript; CO, HPSS, DG, SS and PG: were responsible for data management and analysis; UK and SK: were responsible for the field work including blood sampling and anthropometry; RL: was responsible for laboratory analyses and their quality control; All the authors contributed to and approved the submitted version; HPSS and UK: will act as co-guarantors.

*Funding***:** Indian Council of Medical Research (ICMR); *Competing interests*: None stated.

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