Daily Iron Requirements in Healthy Indian Children and Adolescents

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Objective: This study aimed to define the estimated average requirement and the recommended dietary allowance of iron for Indian children and adolescents. **Methods**: The Estimated average requirement was derived for children aged 1-17y, from the mean bioavailability-adjusted daily physiological iron requirement, which in turn was estimated using a factorial method. This consisted of mean daily iron losses from the body and additional iron required for tissue growth and storage, while also defining the variance of each factor to derive the Recommended dietary allowance. **Results:** The estimated average requirement of iron for children ranged from 5.6 to 11.0 mg/d in children aged 1-9y. For adolescents aged 10-17y, these ranged from 10.8 to 18.4 mg/d and 15.4 to 18.5 mg/d for adolescent boys and girls, respectively. **Conclusion:** New estimates of estimated average requirement for iron in Indian children are presented, and same may be used to inform iron supplementation and food fortification policies.

Keywords: *Anemia, Deficiency, Estimated Average Requirement, Recommended Dietary Allowance*.

Iron is an essential micronutrient for children and adolescents and the current Indian Council of Medical Research (ICMR) Recommended dietary allowances (RDA, 2010) report a daily iron requirement as high as 32 mg/d for adolescent boys [1]. Since the iron density from Indian diet is 9 mg/1000 kCal [1], it would require an extraordinary energy intake of more than 3000 kCal/d to meet the requirement. This has led to the iron fortification of staple foods, anchored to the daily iron requirement of adolescent girls. The combination of a high daily iron-requirement and persisting high anemia prevalence in children and adolescents has led to the launch of both supplementation [2] and multiple staple food fortification programs [3] to overcome the apparent dietary iron deficit. The metric that is used to define the risk of population level nutrient deficiency is the Estimated average requirement (EAR). The RDA is another requirement metric that is defined from the variance of the iron requirement and is the 97.5th percentile of the distribution. The RDA is only applied to individuals and never for populations [4]. The current Indian recommendation [1] provides a single value for the requirement, called RDA. This paper sets out a factorial determination of the EAR and RDA of iron in Indian children and adolescents.

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METHODS

Iron requirements during childhood and adolescence were estimated using a factorial method, based on replacing the iron lost from the body (basal and menstrual) and providing additional iron required for growth and storage. This was then adjusted for the dietary iron bioavailability to derive a mean value (EAR). The RDA was defined as the 97.5th percentile of the distribution of requirements based on the summed variance.

The body weight of the children or adolescents at each year was used to estimate basal iron loss. For children below 9y, the body weight provided by WHO Child Growth Standards (2006) were used [5]. For children from 10-17y, the mean body weight and its distribution was calculated from the WHO reference BMI for age at WHO reference median height for age [5]. This was validated, since the BMI, using the WHO reference weight and the 95th percentile of height at 17y of age from the NNMB data [1], was 21.8 and 22.4 kg/m^2 for girls and boys, which is in the middle of the normal adult BMI range. Since the current ICMR RDA [1] used the 95th

percentile of body weights from the National Nutrition Monitoring Bureau (NNMB), a comparison was made with the WHO body weight values (***Fig.* 1**). Further, the EAR was also calculated using NNMB body weights for comparison with the EAR calculated from the WHO data. For daily increments in body weight, the 50th percentiles of weight were regressed on age to derive the mean weight gain/day.

Details on the values and calculations used for the mean and variance of the basal iron loss, as well as additional iron requirements due to growth related increase in hemoglobin mass, non-storage tissue iron, and storage iron are given in the ***Web Appendix* I.** For adolescent girls, additional iron required to replace that lost during menstruation was based on studies reporting blood and iron loss during menstruation among women (15-50y), as menstrual blood loss during adolescence does not differ from that of women in reproductive age [6]. Iron loss was calculated as the product of the daily blood loss over a 28d cycle, the hemoglobin concentration and the iron content of hemoglobin [7].

The values for each factor were summed to arrive at the distribution of the physiological requirement. For adolescent girls, where the menstrual iron loss was positively skewed, a convolution of normal and log-normal was obtained as the probability distribution of the physiological requirement [7]. As there is no close form available for this convolution, a Monte-Carlo simulation technique was applied to obtain the distribution of the total physiological iron requirement.

Finally, estimates for the EAR in young children and adolescent boys were obtained by adjusting this value for a bioavailability from cereal-based meals, of 6% for children aged 1-9y [8], and 8% for adolescent children aged 10-17y [9]. The iron bioavailability studies were based on the assumption that 80% or 90% of the absorbed iron was incorporated into hemoglobin. The RDA (97.5th percentile) was estimated from the pooled variance of the factors, assuming a normal distribution. Sensitivity analyses were also performed to evaluate differences in the estimate of the physiological iron requirement and the EAR, when the assumptions used varied by 10%.

An additional calculation to estimate an extra allowance of iron required to replenish low body iron stores was done as follows:

For normal iron store size calculation, a value of 5 mg/kg body weight (using the body weights that were taken in the calculations above) was used for healthy children and adolescents [10]. Although the size of the iron store increases more in adolescent boys after 10y, the value of 5 mg/kg was retained for these children as well, as the stores approximated 6 mg/kg in healthy children [10].

This was adjusted for a bioavailability of 6% and 8% for 1-9y and 10-17y, respectively. It is likely that absorption will be up-regulated in iron depleted individuals [11], and therefore, this final estimate of the allowance is conservative.

RESULTS

The basal loss of iron was taken as 14 ± 4.1 µg/kg/d. The annual body weight, obtained from WHO, are presented in ***Table* I; *Fig.* 1** shows these body weights in comparison to those from the NNMB at the 50th and 95th percentile. Up to the age of 10y, the 50th percentile weight from WHO correspond closely to the NNMB 95th percentile. From 10-17y, the 50th percentile weight from WHO was substantially higher, increasing with each year of age, until a maximum difference of about 10 and 3 kg for boys and girls, respectively. The co-efficient of variation (CV) of weight ranged from 12.3 to 18.5% for different ages.

The mean (SD) menstrual iron loss in adolescent girls was 0.52 (0.69) mg/d [7]. The mean blood volume expansion, along with mean tissue mass expansion (and their respective SD) for ranges of age (1-9y for both sexes and 10-17y separately for boys and girls) are reported in ***Web Table* I**.

The EAR ranged from 5.6 to 11.0 mg/d in children aged 1-9y (***Table* I)**, with RDA ranging from 7.3 to 16.0 mg/d. The physiological iron requirement is also presented in ***Table* I**. The EAR in boys aged 10-17y ranged from 10.8 to 18.4 mg/d, due to a higher weight. The EAR of girls between the ages of 10-17y was higher at earlier ages because of additional menstrual losses and ranged from 15.4 to 18.5 mg/d. In both sexes, the RDA was higher (***Table* I**), and for adolescent boys, ranged from 14.6 to 26.4 mg/d, while for adolescent girls it ranged from 32.3 to 36.9 mg/d. The latter was because of the high variance in menstrual blood losses. Sensitivity analyses, using changes of 10% in the values used in the factorial analysis showed that the major contributing factor to the EAR was the bioavailability term.

Since the present Indian RDA used the 95th percentile weight from NNMB, a comparison of the EAR and RDA values using the WHO and the NNMB weight reference is provided in ***Web Table* II**. The daily allowance that would be required for replenishing iron stores over 1year, for each age, assuming that the iron stores of the children were depleted to 50% of the normal value, is provided in ***Table* II**. The allowance ranged from 1.1 to 3.2 mg/d in

TABLE I ESTIMATED EAR AND RDA FOR CHILDREN (1 TO 9 YEARS) AND ADOLESCENTS (10 TO17 YEARS) AND COMPARISON TO ICMR 2010 RECOMMENDATION

Age (y)	*Sex*	*Weight (kg)*	*Physiological iron requirement**	*EAR (mg/d)#*	*RDA (mg/d)$*	*Physiological ‘“ iron requirement*	*RDA - ICMR 2010 (mg/d)^*
1	Both	9.3	0.34	5.6	7.3	0.45	9
2	Both	11.8	0.39	6.5	8.5	0.45	9
3	Both	14.1	0.43	7.1	9.5	0.45	9
4	Both	16.2	0.46	7.6	10.4	0.63	13
5	Both	18.3	0.49	8.2	11.3	0.63	13
6	Both	20.3	0.48	8.9	12.4	0.63	13
7	Both	22.6	0.51	9.5	13.4	0.77	16
8	Both	25.2	0.54	10.2	14.6	0.77	16
9	Both	28.2	0.56	11.0	16.0	0.77	16
10	Boys	31.2	0.77	10.8	14.6	1.05	21
11	Boys	34.7	0.79	11.5	15.7	1.05	21
12	Boys	39.0	0.84	12.6	17.3	1.05	21
13	Boys	44.4	0.90	13.8	19.2	1.60	32
14	Boys	50.6	1.00	15.5	21.8	1.60	32
15	Boys	56.5	1.08	16.8	23.8	1.60	32
16	Boys	61.3	1.15	17.8	25.3	1.37	28
17	Boys	64.9	1.22	18.4	26.4	1.37	28
10	Girls	31.9	1.13	15.4	32.3	1.33	27
11	Girls	36.3	1.17	15.9	33.0	1.33	27
12	Girls	41.2	1.21	16.4	33.8	1.33	27
13	Girls	46.0	1.24	16.9	34.5	1.36	27
14	Girls	50.0	1.27	17.4	35.3	1.36	27
15	Girls	52.8	1.29	17.9	35.9	1.36	27
16	Girls	54.7	1.30	18.2	36.5	1.30	26
17	Girls	55.8	1.32	18.5	36.9	1.30	26

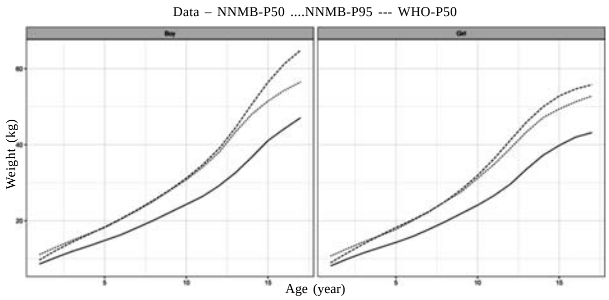
*ICMR: Indian Clinical of Medical Research; EAR: Estimate average requirement; RDA: Recommended dietary allowance. *Physiological iron requirements before adjusting for diet iron bioavailability- present study; #EAR obtained after adjusting for a bioavailability of 6% for children 1-9y of age, and 8% for older children; 97.5^{th} percentile of the distribution of requirements; ‘“Physiological iron requirements before adjusting for diet iron bioavailability- ICMR 2010 [1]; ^The ICMR 2010 RDA of iron [1].*

children aged 1-9y, from 3.6 to 5.6 mg/d and 2.7 to 4.8 mg/d in adolescent boys and girls aged 10-17y, respectively.

DISCUSSION

This study presents newly calculated EAR and RDA values of iron in Indian children. The EAR should be used in assessing population level estimates of the adequacy or inadequacy of the diet, while the RDA should be used with caution for individuals. The present study EAR estimation is also higher than other international estimates such as the Institute of Medicine [12], which used an iron bioavailability of 18%, largely from heme sources, lower values for tissue iron stores, and no requirement for iron storage after nine year of age.

To validate the present study EAR value, the estimated risk of dietary inadequacy was estimated from the NNMB [13] data of daily iron intake of children aged 1-3 year from rural UP, and the present study EAR for same age (average of 6.4 mg/d). In the same survey, the risk of dietary iron inadequacy was determined to be 49%. In another recent study on under - 5 children in 25 districts of UP [14], the prevalence of iron deficiency was 62%, which is reasonably close to the calculated prevalence of risk of dietary inadequacy (49%) in a similar population. Similarly, the prevalence of risk of dietary iron inadequacy was 54% for adolescent girls from UP [1], while the



NNMB P_{50} - 50th percentile of NNMB data [1]; NNMP P_{95} - 95th percentile of NNMB data [1]; WHO P_{50} - 50th percentile of WHO data [5].

FIG. 1 *Comparison of body weights derived from 50th percentile of WHO values with NNMB 50th and 95th percentile, between ages of 1-17y.*

prevalence of iron deficiency based on serum ferritin was 41% (in UP and Bihar girls residing in the slums of Delhi) [15]. This kind of validation needs to be repeated with more studies.

There are several explanations for the differences in the present study and the current Indian RDA [1] estimates. First, the current Indian RDA used a value of 5% for the dietary bioavailability of iron in children and adolescents [1], in contrast to the present estimate, which used values of 6% and 8%, respectively [8,9]. Second, in adolescent girls, the Indian RDA used a single mean estimate for menstrual iron loss in the factorial calculation; however, as this distribution is positively skewed, the mean value could have overestimated this factor. Third, for adolescent boys, the Indian recommendation [1] considered that they would need to build an iron store of 810 mg over the age period of 13-17y. This resulted in an additional iron allowance of 8 mg/d (after adjusting for a bioavailability of 5%), which was added to the current Indian RDA estimate [1]. This assumes that the healthy adolescent boys had zero stores when entering this age range, and a high value for the iron store at this age, compared to similar estimates in other healthy populations [10]. Similarly, for adolescent girls, an additional allowance of 3 mg iron/d was added to the current Indian RDA estimate [1]. In the present study, the requirement was explicitly meant for healthy (not deficient) children. However, the present study did consider an extra allowance for replenishing iron stores over a year.

TABLE II ADDITIONAL IRON REQUIREMENT TO REPLENISH BODY IRON STORES OVER ONE YEAR

Age (y)	*Sex (mg)**	*Iron storage*	*50% deficit (mg)#*	*Additional iron (mg/d)$*
1	Both	47	23	1.1
2	Both	59	30	1.3
3	Both	71	35	1.6
4	Both	81	41	1.9
5	Both	91	46	2.1
6	Both	102	51	2.3
7	Both	113	57	2.6
8	Both	126	63	2.9
9	Both	141	70	3.2
10	Boys	156	78	3.6
11	Boys	173	87	3.0
12	Boys	195	97	3.3
13	Boys	222	111	3.8
14	Boys	253	127	4.3
15	Boys	282	141	4.8
16	Boys	306	153	5.2
17	Boys	324	162	5.6
10	Girls	160	80	2.7
11	Girls	181	91	3.1
12	Girls	206	103	3.5
13	Girls	230	115	3.9
14	Girls	250	125	4.3
15	Girls	264	132	4.5
16	Girls	273	137	4.7
17	Girls	279	139	4.8

**Iron storage was calculated using a value of 5 mg/kg body weight [10]. For each year of age body weight was taken from Table II; #This is the 50% deficiency from normal iron stores; $The additional iron required to meet the deficiency in iron stores in a period of one year.*

The present EAR has an important bearing on the regulatory recommendations for the fortification of iron in staple foods, which is anchored to the requirement of adolescent girls (27 mg/d) [1]. If the present EAR of 18.5 mg/day in adolescent girls were used, it would mean a lower fortification level. However, there are knowledge gaps of limited studies on menstrual iron loss and a wider estimation of iron absorption with different meals in

WHAT THIS STUDY ADDS?

- An estimate of the Estimated average requirement (EAR) and Recommended dietary allowance (RDA) of iron for Indian children and adolescents is provided, which informs policies of fortification and supplementation.

different age groups. The EAR should be used in evaluations of dietary iron inadequacy, and of iron supplementation and food fortification.

Contributors: SG, SS: data compilation and literature review. SG, TT: statistical analysis used in the manuscript; NS, HPS, AVK: physiological aspects of the analysis. All authors contributed equally to analyzing the data and drafting the manuscript. AVK: approved the final draft of the manuscript.

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