Original Article

Anemia and intestinal parasite infection in school children in rural Vietnam

Huong Thi Le PhD[1,2], Inge D Brouwer PhD[2], Hans Verhoef PhD[3], Khan Cong Nguyen PhD[4] and Frans J Kok PhD[2]

[1]*The Nutrition Department, Hanoi Medical University, Vietnam*
[2]*The Division of Human Nutrition, Wageningen University, Netherlands*
[3]*Cell Biology and Immunology Group, Wageningen University, Netherlands*
[4]*The National Institute of Nutrition, Hanoi, Vietnam*

Objectives: This study hypothesized that besides iron deficiency, intestinal parasites infection is also a determinant of anemia in schoolchildren in rural Vietnam. **Methods**: 400 primary schoolchildren from 20 primary schools in Tam Nong district, a poor rural area in Vietnam, were randomly selected from enrolment lists. Venous blood (5ml) was collected in a cross sectional study and analyzed for hemoglobin (Hb), serum ferritin (SF), serum transferrin receptor (TfR), serum C-reactive protein (CRP) and total immunoglobulin E (IgE). Stools samples were examined for hookworm, *Trichuris*, and *Ascaris* infection. Logistic regression was used to assess the effect of intestinal parasites on anemia. **Results**: The prevalence of anemia (Hb<115g/L) was 25%. Iron deficiency (TfR >8.5mg/L) occurred in 2% of the children. The prevalence of intestinal parasites was 92% with the highest prevalence for *Trichuris* (76%) and *Ascaris* (71%). More than 30% and 80% of the children showed an elevated CRP (≥ 8 mg/L) and IgE (> 90 IU/mL) concentration. Anemia status was borderline significantly associated with SF and not associated with TfR and CRP. The prevalence odds ratio for *Trichuris* infection was 1.96 (95%CI 1.07-3.59) and 2.00 (95% CI 1.08-3.65) with iron deficiency reflected by TfR and SF, respectively. **Conclusion**: Anemia is highly prevalent among schoolchildren in Vietnam but may not be associated with iron deficiency. *Trichuris* infection is associated with a doubled risk of anemia, not mediated through iron deficiency. Chronic infection may play a role in anemia, but needs further investigation.

Key Words: iron deficiency, anemia, parasite, children, Vietnam

INTRODUCTION

Anemia is a significant public health problem in Vietnam. The 2000 Nutrition Risk Factor Survey showed that the anemia prevalence was 34% in children under five years of age and 25% in women.[1] No national representative data are available on the prevalence of anemia among primary schoolchildren in Vietnam, however, several local studies showed an anemia prevalence of around 30%.[2, 3] Anemia in children can be caused by iron deficiency and by health factors such as parasite infection[4] or causes of anemia, being genetic disorders such as the hemoglobinopathies and thalassemias.[5, 6] Schoolchildren carry the heaviest burden of intestinal parasitic infection.[7] Studies in primary schoolchildren in sub-urban Hanoi and Nam Ha province showed high prevalences of intestinal parasites of 88.4% and 92.9%, respectively.[3, 8] Many studies have shown that hookworm causes chronic intestinal blood loss;[9] blood loss can also occur in *Trichuris* infection,[10, 11] but probably becomes significant only in severe infection.[12] Iron deficiency is the predominant cause of anemia in all age groups.[13] However, the possibility that infection could also play an important role has received increasing attention during the last few years.[13] We hypothesize that both iron deficiency and intestinal parasite infection are associated with anemia in schoolchildren in rural area in Vietnam. Using data from a survey among schoolchildren, we assessed the iron status and parasitic infection and tested whether our data are consistent with this hypothesis.

METHODS

Study area and population

This study was conducted in October 2003 in Tam Nong district, Phu Tho province, a rural agricultural based area located 90 km northwest of Hanoi, Vietnam. Tam Nong includes 20 communes with a total population of 79552. The school lists of all children in grade one to three in all 20 primary schools in Tam Nong district with complete information on date of birth and gender were collected. 400 primary schoolchildren were randomly selected from the lists of 20 schools. Children were invited for the study and their parents were asked for an informed consent. The study was approved by the Scientific Committee of the National Institute of Nutrition and the Ethics Committee of Hanoi Medical University - Ministry of Health.

Corresponding Author: Mrs. Huong Thi Le, No 41 lane 101, Pham Ngoc Thach str Dongda, Hanoi, Vietnam
Tel: 84-4-5744576; Fax: 84-4-7337955
Email: huong.lethi@wur.nl; donghuong@fpt.vn
Manuscript received 8 November 2006. Initial review completed 27 January 2007. Revision accepted 28 February 2007.

Data collection

Interviews with parents were performed to obtain information about background characteristics of children as well as the children's past and present illnesses.

Body weight and height were measured using standardized procedures[14] and recorded as the midpoint of duplicate measurements. Children's weight was measured to the nearest 100 gram using an electronic scale (Seca, 890, UK) and standing height was measured to the nearest 1 mm with a wooden stadiometer (CMS equipment Ltd, UK). The subjects wore minimum clothing and no shoes. Age was calculated from the birth date in the school records based on birth certificates.

Blood samples (5 ml) were collected by venipuncture, 20µl whole blood was pipetted immediately before coagulating into a tube containing 5.0 ml of Drabkin's reagent with a Sali pipette for hemoglobin measurement, the remaining blood was allowed to clot for 30 minutes at room temperature, centrifuged at 3000 x g for 15 minutes and transferred to 5 plastic labelled vials (Eppendorf tubes 0.5ml). The vials were stored at -30^{o}C until serum ferritin (SF), transferrin receptor (TfR), C-reactive protein (CRP) and immunoglobulin E (IgE) analysis.

For assessment of intestinal parasites infection, containers for collection of stools were distributed to each class and children were asked to collect and deliver a sample of their feces to school the next day. In case some children were unable to return a sample, one of the field workers returned the next day to collect the rest of the samples at the schools. 394 children returned a faecal sample.

Food consumption of the children was investigated by a 24-h recall[15] of two non-consecutive days among a subsample of 60 children in two schools (51 children who were included in the cross sectional study complemented with 9 children randomly selected from the school lists). The 24-h recall was done through the parents in the presence of the children. The 24-h recall covered all foods and drinks consumed by the child during the previous day, from the early morning the day before the interview till the early morning of the day of interview.[15]

Laboratory analysis

SF and TfR, CRP and IgE analysis was carried out at the National Institute of Nutrition and the laboratory of Hanoi Medical University. A sample of 43 and 41 blood samples were reanalyzed in SHO (Stichting Huisartsenlaboratorium Oost, Velp, The Netherlands) for TfR and SF for quality control. Hemoglobin concentration was measured in the whole blood within 12 h of sampling by cyanmethemoglobin method using Sigma KIT. The coefficients of variation (CV) of intra-essays and inter-essays was 4.0 ± 1.2% and 5.0 ± 2.0% respectively.

In Vietnam, SF and TfR were performed by an enzyme-linked immunosorbent assay (ELISA) method (Ramco Laboratories, Inc, Houston, TE, Catalogue numbers S-22 and TF-94), with inter-assay variabilities of 4-7% and 4-8%, respectively. For the re-analysis of these indicators in the Netherlands, an ELISA (The Access, Beckman) was used for SF and the Behring N Latex OQ TC11 method was used for TfR and run on a Behring Nephelometer (BNII). Serum CRP was measured by nephelometry using Epress plus, with an inter-assay variability of 4-8 %. Serum IgE was determined by ELISA using the Kallestad Total IgE Microplate Kit from GmbH - Germany, with an inter-assay variability of 4-6 %. Stools samples were examined by using the Kato-Katz technique – a cellophane faecal thick smear method.[16] hookworm, *Trichuris trichura,* and *Ascaris lumbricoides* eggs were counted. A 10% sub sample of smears was re-examined for quality control.

Data analysis

Anthropometric indices were calculated using the WHO/NCHS reference data.[17] Being wasted, stunted and underweight is defined by z-scores <–2SD for weight-for-height, height-for-age and weight-for-age, respectively. The nutrients and iron intake was calculated using the VBS BAS Nutrition Software programme,[18] using a modified Nutritive Composition Table of Vietnamese foods.[19] Absorbable iron is calculated assuming heme-iron bioavailability of 23% and non-heme iron bioavailability of 5%.[20] This was compared to the FAO/WHO recommended requirement of iron.[21]

Anemia was defined as hemoglobin concentrations <115g/L.[22] Iron deficiency was defined as SF <12 µg/L, [(22)] and tissue iron deficiency was defined as TfR>8.5 mg/L[23] measured with the Ramco test and TfR >1.76mg/dL measured with the Behring N Latex method (reference from the laboratory). Serum CRP concentration was used as an indicator of possible infection and/or inflammatory diseases and considered to be abnormal when ≥ 8 mg/L.[24] Serum IgE concentrations, which are elevated in cases of high fever, allergy, and presence of parasitic infection were considered to be elevated if > 90 IU/mL in children 6-9 years of age.[25] Severity of intestinal worm infections was expressed as the number of eggs/g feces using the WHO classification system.[26]

Statistical analyses

Data were entered into the computer, cleaned and managed using Epi Info version 6,[27] and analyzed using SPSS 11.0 for windows (SPSS Inc., Chicago IL, USA).[28] Differences in hemoglobin concentrations and anemia were assessed by age (using four age groups 5, 6, 7, and 8 years), gender, elevated/normal CRP and elevated/normal IgE by using the independent sample t-test for continuous variables and the chi-square test for proportions. To assess the association between worm infection and indicators of iron and anemia status, we compared children with and without different types of worms with respect to their hemoglobin, TfR and SF. To further explore the association between anemia, worm infection and iron deficiency, logistic regression was used to assess the effect of intestinal worms on anemia. Anemia was modelled as a function of type of worm infection (*Ascaris, Trichuris,* hookworm), and iron deficiency as reflected by TfR (model 1) or SF (model 2). Gender, age, serum CRP and IgE concentration were considered as potential confounding variables.

RESULTS

Descriptive statistics for the study population are provided in Table 1. The prevalence of anemia (Hb<115g/L)

Table 1: Characteristics of the study population

Variables	Population estimate (n=400)
Age in months†	87.8 ±10.5
Gender (Boys)%†	50.3
Hemoglobin concentration g/L †	120 ±8.3
Serum transferrin receptor mg/L †	5.5± 1.27
Serum ferritin µg/L‡	50.8 (34.0-73.2)
Prevalence of anemia	25
(Hemoglobin concentration <115g/L), %	
Prevalence of iron deficiency	
(Serum ferritin <12µg/L), %	0.5
(Serum transferin receptor >8.5 mg/L), %	2.0
Prevalence of iron deficiency (excluded CRP> 8 mg/L)	
(Serum ferritin <12µg/L), %	0.6
(Serum transferin receptor >8.5 mg/L), %	1.9
Prevalence of children with inflammation	30.5
(Serum C-reactive protein ≥ 8 mg/L), %	
Prevalence of IgE elevated	80.3
(Serum IgE >90 IU/mL), %	
Nutrition status	
WAZ†	-1.7 ± 0.7
HAZ†	-1.4 ± 0.9
WHZ†	-1.3 ± 0.7
Prevalence of malnutrition	
Wasting (WHZ<-2SD), % (95% CI)	15.0 (11.6-18.4)
Stunting (HAZ<-2SD), % (95% CI)	25.5 (21.3-29.7)
Underweight (WAZ<-2SD), % (95% CI)	41.5 (36.7-46.3)
Parasite infection (n= 394)§	92 (89-94)
Ascaris only %, (95% CI)	15 (12-19)
Trichuris only%, (95% CI)	19 (15-23)
Ascaris and *Trichuris* %, (95% CI)	52 (47-57)
Ascaris, *Trichuris* and hookworm, %	4 (2-6)
Trichuris + hookworm, %, (95% CI)	1 (1-2)
Hookworm only%, (95% CI)	1 (1-2)
Daily intake†,¶	
Energy intake (MJ)	5.1 ±1.7
Carbohydrate intake (gr)	222 ± 77.5
Protein intake (gr)	41.6 ± 18.5
Fat intake (gr)	16.6 ± 11.0
Vitamin C intake (mg)	35.1 ± 44.7
Iron intake (mg)	7.5 ± 4.0
Contribution to iron intake, %	
Rice	37
Animal food	15

†Mean ± SD; § Data available for 394 children; ‡ Median (25 and 75 percentile); ¶ Data available for 60 children

was 25% and mean hemoglobin concentration was 120 ± 8.3 g/L. Iron deficiency defined as serum transferrin receptor >8.5mg/L occurred in 2% of the children (as assessed using the RAMCO test). The prevalence of infection with intestinal parasites was 92% with the highest prevalence for *Trichuris* (76%) and *Ascaris* (71%) with most children (52%) being infected by both parasites. Most of *Ascaris* infection was moderate (57%), and 68% of *Trichuris* infection was light. Only 6 % of the children had hookworm infection. More than 30% and 80% of the children had elevated concentrations of CRP and IgE, respectively. The prevalence of malnutrition was very high with 15.0%, 25.5% and 41.5% of the children being wasted, stunted and underweight, respectively. The average daily energy intake was 5.1 ± 1.7 MJ which corresponds to 68% of the recommended nutrient intake for this age group (7.5 MJ).[29, 30] A major part of the energy intake was from rice (64%). The daily iron intake was 7.5 ± 4.0 mg which corresponds to 46% of the Recommended

Table 2. Hemoglobin concentrations and anemia prevalence by age, gender, inflammation and iron deficiency status among primary schoolchildren in rural Vietnam

Variable	Hb-concentration, g/L (mean ± SD)	Hb < 115g/L (%)
Age, yr		
5 (n=26)	119 ± 6.9	38.0
6 (n=125)	120 ± 8.7	24.4
7 (n=126)	119 ± 7.5	24.6
8 (n=123)	201 ± 8.9	23.6
Gender		
Boys (n=201)	119 ± 8.4	28.8*
Girls (n= 199)	120 ± 8.2	21.1
C-reactive protein		
Elevated (≥ 8 mg/L)	119 ± 8.2	27.0
Normal	120 ± 8.3	24.1
IgE		
Elevated (>90 IU/mL)	119 ± 8.5	25.0
Normal	121 ± 7.5	19.8

* p=0.047

Table 3. Serum transferrin receptor and serum ferritin by elevated and non-elevated of CRP and IgE

	Serum transferrin receptor	Serum ferritin
C-reactive protein		
Elevated (≥ 8 mg/L)	5.3 ± 1.3	55.6 ± 33.9*
Normal	5.5 ± 1.3	66.7 ± 38.2
IgE		
Elevated (>90 IU/mL)	5.5 ± 1.3	60.7 ± 36.9**
Normal	5.3 ± 1.1	52.1 ± 28.9

* p= 0.004; * * p= 0.05

Nutrient Intake (16.2 mg/day) calculated based on age distribution of study sample.[21, 30] A major part of the iron intake is provided by rice (37%) and only 15% is from animal sources. Amount of absorbable iron was 0.58 mg, just below the FAO/WHO recommended daily iron requirement of 0.63 mg for this age group.[21]

The youngest group showed the highest anemia prevalence (**Table 2**). Compared to girls, boys had a higher prevalence of anemia (28.8% compared to 21.1%) and a slightly lower hemoglobin concentration (1.4 g/L, 95% CI = -3.1 to 0.19). Although not significant, children with elevated IgE showed a slightly lower hemoglobin concentration and higher prevalence of anemia (**Table 2**). Children with elevated IgE had a higher concentration of SF compared to those with a non elevated IgE while children with elevated CRP had a lower SF than non elevated children. No differences were found in TfR between elevated and non elevated CRP and IgE groups (**Table 3**). Children infected with hookworm and *Trichuris* showed a lower hemoglobin concentration and a higher prevalence of anemia (**Table 4),** although not statistically significant for hookworm. This was further supported in the logistic regression models showing a prevalence odds ratio for *Trichuris* infection of 1.96 (95% CI 1.07-3.59) and 2.00 (95%CI 1.08-3.65) with iron deficiency reflected by TfR and SF, respectively. (**Table 5)**. *Ascaris* and hookworm were not significantly associated with hemoglobin concentrations or anemia prevalence. No association was found for TfR, SF, CRP concentration with parasite infection, but there was a relationship between *Trichuris* infection and IgE **(Table 4).** There was a borderline significant association between SF and anemia (p=0.05), but no association was found for TfR concentrations with anemia after taking into account CRP and IgE concentration. IgE was significantly associated with anemia. (**Table 5)**.

DISCUSSION

In the present study 25% of children were found to be anaemic (Hb<115g/L). The low percentages of children having SF below 12 μg/L (0.5%) and TfR above 8.5 mg/L (2%), indicate that there is very low iron deficiency anemia among our study population. This was surprising to us as to our knowledge this is the first study in Vietnam showing a high anemia prevalence of 25% with very low iron deficiency. Moreover, our food consumption data indicate that iron intake of the children was marginal and a previous study in the area showed improvement of anemia status of pregnant women and young children (from 25.4% to 12.5% and 68% to 31.7%) after iron supplementation.[31] We were concerned about our blood measurements but reanalysis of subsamples at SHO (Stichting Huisartsenlaboratorium Oost, Velp, the Netherlands) revealed similar results.

SF is shown to increase during infection, giving false negative results for iron deficiency in infection prone populations.[32] For this reason, it has been suggested to use a higher cut–off value for SF to determine iron deficiency in populations where infections and /or inflammatory diseases are highly prevalent.[33, 34] In our study, 30.5% of children showed elevated CRP indicating presence of infection which may lead to underestimation of iron deficiency using SF. However, excluding children with elevated CRP in our study did not reduce SF. Data from our study show a borderline significant association between anemia and SF after adjusting for CRP (**Table 5**), indicating that there is a small contribution of iron deficiency to anemia.

TfR was not associated with anemia (**Table 5**). Serum TfR is considered to be a more reliable measure of iron status than SF in settings with a high prevalence of acute infections.[35] However, few large published clinical trials among adults in developing countries[36, 37] are available and even fewer studies with children. The diagnostic cut-offs for TfR used to identify iron deficiency were derived from studies in adults.[38] These cut-offs may not apply to children due to their increased erythropoeisis during growth.[39] The discriminating power of TfR in presence of infection has been questioned.[35, 40] Elevated TfR differentiates iron deficiency anemia from anemia of chronic infection, but normal TfR in the presence of chronic infection can not exclude iron deficiency.[35, 41] Also in our study the (small) role of iron deficiency in anemia as indicated by the association of anemia and SF was not detected by TfR suggesting the presence of chronic infection.

The presence of anemia with a low prevalence of iron deficiency suggests that important causes of anemia beyond iron deficiency exist. A study in schoolchildren in North-East Thailand also found a high prevalence of anemia without iron deficiency, with hemoglobinopathies, suboptimal vitamin A status and age as the major predictors of hemoglobin concentration.[42] Another study in school-aged children in Alaska showed 15% anemia with 8% being iron deficient, with bacterial infection (*Helicobacter pylori*) as a possible contributor to anemia.[43] Data from a sub-study among schoolchildren in the same age group in the same study area indicated that probably both thalassemia and vitamin A were not causes of anemia in our population as thalassemia was only present in 7 % and vitamin A deficiency in 8% in the population of this sub-study.[44] Other nutrient deficiencies associated with anemia include deficiencies of vitamins B6, B12, riboflavin, and folic acid[45] although not all of the causal pathways are yet clearly understood. Vitamin B12 and folic acid deficiency are associated with an increased TfR,[14] but we did not observe elevated TfR levels in our study population. The role of other nutrients could not be verified in the present study. Malaria, another main cause of anemia,[46, 47] does not exist in our study area.

In our study the presence of *Trichuris* infection was associated with a doubled risk of having anemia, and

Table 4: Iron status and inflammation by type of parasite infection among schoolchildren in rural Vietnam

	Parasite		*Ascaris*		*Trichuris*		Hookworm	
	Infection (n= 361)	No infection (n= 33)	Infection (n= 281)	No infection (n= 113)	Infection (n= 298)	No infection (n= 96)	Infection (n= 23)	No infection (n= 371)
Hemoglobin concentration, g/L†	120±8.3	120±8.4	120±8.4	120±8.1	119±8.5	121±7.6*	118±7.1	120±8.4
Anemia (hemoglobin <115 g/L), %	25.5	24.2	24.9	26.5	28.2	16.7**	30.4	25.1
Serum transferrin receptor, mg/L†	5.5±1.3	5.5±1.1	5.5±1.4	5.4±1.1	5.5±1.3	5.5±1.3	5.1±1.2	5.5±1.3
Serum ferritin, mg/L‡	49.2 (33.3-72.2)	58 (42.7-93.5)	48.6 (33.0-72.2)	55.1 (38.0- 77.3)	50.5 (34.4-73.0)	54.9 (36.9-82.6)	44.4 (30.3-72.2)	51.0 (34.4-75.6)
CRP elevated, % (>8 mg/L)	30.2	30.3	29.2	32.7	29.5	32.3	34.8	29.9
IgE elevated, % (>90 IU/mL)	81.4	63.6***	81.9	75.2	82.6	71.9****	87	79.5

* p= 0.037(Difference between infected and not infected, independent sample t-test); ** p= 0.015 (Difference between infected and not infected, chi-square test); *** p= 0.017 (Difference between infected and not infected, chi-square test); ****p= 0.019 (Difference between infected and not infected, chi-square test); † Mean ±SD; ‡ Median (25th,75th percentile)

Table 5: Prevalence ratio for anemia of parasite infection and indicators of iron status of Vietnamese schoolchildren

Logistic regression Outcome variable: Anemia status			**Logistic regression** Outcome variable: Anemia status		
Variable	Prevalence ratio†	*p*	Variable	Prevalence ratio†	*p*
Trichuris	1.96 (1.07-3.59)	0.03	Trichuris	2.00 (1.08 – 3.65)	0.02
Hookworm	1.24 (0.49-3.16)	0.65	Hookworm	1.15 (0.45 – 2.93)	0.77
Ascaris	0.86 (0.52-1.44)	0.58	Ascaris	0.85 (0.51 – 1.42)	0.53
Transferrin receptor	1.08 (0.91-1.30)	0.37	Ferritin	0.99 (0.98 – 1.00)	0.05
Gender	0.65 (0.43-1.00)	0.12	Gender	0.72 (0.45 – 1.16)	0.18
Age	0.92 (0.79-1.19)	0.51	Age	0.95 (0.72 - 1.24)	0.69
IgE	1.00 (1.00-1.00)	0.01	CRP	1.02 (0.99 - 1.05)	0.24
			IgE	1.00 (1.00 - 1.00)	0.01

† Prevalence of Odds Ratio (95% CI)

although our study reconfirms the role of *Trichuris* infection with anemia reported in other studies,[10, 11] we surprisingly found that *Trichuris* is related to anemia not only in severe infection but also in mild infection. Although literature indicates there is indeed a strong association of hookworm with increased prevalence of anemia and reduced iron stores,[9, 48, 49] our study did not find this association probably due to low prevalence of hookworm and low worm burden in the study population. *Ascaris* infection showed no association with anemia, which is in agreement with other previous studies.[50, 51]

The mechanism of the association between *Trichuris* and anemia in this study is not clear. *Trichuris* is suggested to be associated with anemia mediated through iron deficiency caused by blood loss or anorexia.[11] However, in our study we also did not see an association between *Trichuris* infection and iron deficiency. This may indicate that the association between *Trichuris* infection and anemia found in this study might be due to the presence of another un-identified factor associated with both *Trichuris* and anemia. We did not see an association between *Trichuris* infection and (acute) infection as measured by CRP concentration, but there was a positive association with IgE concentration. Faulkner et al suggested that the high IgE concentration may indicate immunity to *Trichuris* infection which may explain the absence of an association with CRP.[52] However, including IgE in the regression analysis model did not change the association between *Trichuris* infection and anemia.

In absence of an association between CRP and SF, the high SF levels in our population may indicate chronic infection as CRP is a good measure of acute infection or inflammation but less appropriate when conditions are chronic.[53] However, SF in our population was much higher compared to the 50^{th} percentile SF value (28.7 μg/L) for the age group 6-9 years in NHANES III,[14] being close to the 90^{th} percentile level of 55.9 μg/L and elevated IgE was associated with higher SF concentration. The high levels of SF and IgE and their association with anemia in our study may suggest that chronic infection may play a role in anemia in our population. The seasonal burden of infections in developing countries has been recognized for many years by agricultural and health professionals.[54] Mild inflammatory conditions such as upper-respiratory infections and otitis media, which remain common in early childhood, may contribute to anaemia.[13] However, the role of seasonal chronic infections in anaemia in our study population needs to be further investigated.

In conclusion, anemia is highly prevalent among schoolchildren in Vietnam, but may not be associated with iron deficiency. *Trichuris infection* is associated with a doubled risk of anemia, but the mechanism is not clear and needs further investigation. High levels of SF and IgE may suggest that chronic infection may play a role in anemia in our children. Further research needs to be carried out to confirm this.

ACKNOWLEDGEMENTS

This study was funded by an Ellison Medical Foundation grant and the Ministry of Education and Training, Vietnam. HV is supported by Netherlands Organisation for Scientific Research NWO/WOTRO (grant number WAO 93-441). The authors would like to acknowledge the assistance of the Directors and teachers from 20 schools and Directors and staff of the Education Department in Tam Nong district Phu Tho province.

AUTHOR DISCLOSURES

Huong Thi Le, Inge D Brouwer, Hans Verhoef, Khan Cong Nguyen and Frans J Kok, no conflicts of interest.

REFERENCES

1. Ninh NX, Khan NC, Khoi HH. Micronutrient deficiencies and strategies for their control in Vietnam. ln:20 years of prevention and control of Micronutrient Deficiency in Vietnam. Medical Publishing House, Hanoi, Vietnam. Ninh NX , Khan NC, Khoi HH , Lam NT eds, 2001:24-33.
2. Hoa DT. Effect of fortified biscuit with vitamin A and iron on vitamin A status and anemia in primary school children in sub- urban Vietnam. PhD thesis, Hanoi: Hanoi Medical University, 2002.
3. Le HT. Nutritional status and related factors of primary school children in Hanoi and sub urban Hanoi. Master thesis, Hanoi: Hanoi Medical University, 1999.
4. INACG. Guidelines for the eradication of iron deficiency anemia. A report of the International Nutritional Anemia Consultative Group (INACG). New York, Washington, DC: Nutrition Foundation, 1997.
5. INACG. Anemia, iron deficiency and iron deficiency anemia. Committee. ILSI, ed. Washington, USA: ILSI Research Foundation, 2002.
6. Dugdale M. Anemia. Obstet Gynecol Clin North Am. 2001;28:363-81.
7. Fernando S, Goonethilleke H, Weerasena K, Kuruppuarachchi ND, Tilakaratne D, Silva de D, Wickremasinghe AR. Geo-helminth infections in a rural area of Sri Lanka. Southeast Asian J Trop Med Public Health. 2001;32:23-6.
8. Khanh N. Effectiveness of de - worming every 6 months to the physical growth and learning capacity of primary school children. Hanoi Medical University, 2000.
9. Crompton D. The public health importance of hookworm disease. Parasitology. 2000;121:S39-S50.
10. Layrisse M, Aparcedo L, Martinez C, Roche M. Blood loss due to infection with Trichuris trichiura. Am J Trop Med Hyg. 1967;16:613-9.
11. Stephenson LS, Holland CV, Cooper ES. The public health significance of Trichuris trichiura. Parasitology. 2000;121:S73-S95.
12. Stephenson L. The impact of helminth infection on human nutrition. London: Taylor and Francis, 1987.
13. Yip R, Dallman PR. The roles of inflammation and iron deficiency as causes of anemia. Am J Clin Nutr. 1988;48:1295-1300.
14. Gibson RS. Principles of nutrition assessment. Second edition ed. Oxford: Oxford University Press, 2005.
15. Cameron M, Staveren W van. Manual on methodology for Food Consumption Studies. Oxford: Oxford University Press, 1988.
16. WHO. Basic laboratory methods in Medical Parasitology, Geneva: World Health Organization, 1991.
17. WHO. Physical status the use and interpretation of anthropometry. WHO Technical Report Series 854. Geneva: World Health Organization, 1995.
18. BAS. Software programmes KOMEET 4.0.55, 2003. ORION 4.0.27, 2002. FOOD GROUP KOMEET 4.0.55, 2003. ORION 4.0.27, 2002. FOOD GROUP 4.0.22, 2004. TOPNUT 4.0.15,2002. VBS Manager 4.0.37, 2002.

19. NIN/MOH. Nutritive composition table of Vietnamese foods. Medical Publishing House, Hanoi, Vietnam 2000.
20. Tseng M, Chakraborty H, Robinson DT, Mendez M, Kohlmeier L. Adjustment of iron intake for dietary enhancers and inhibitors in population studies: biovailable iron in rural and urban residing Russian women and Children. J.Nutr. 1997;127:1456-1468.
21. FAO, WHO. Human vitamin and mineral requirements.Report of a joint FAO/WHO expert consultation. Bangkok, Thailand. Rome: FAO, Food and Nutrition Division, 2001.
22. WHO. Iron deficiency anaemia: Assessment, prevention and control. Geneva: World Health Organization, 2000.
23. Skikne B, Flowers C, Cook JD. Serum transferrin receptor: a quantitative measure of tissue iron deficiency. Blood. 1990;75:1870-6.
24. Hoffbrand A, Pettit J. Essential haematology. Oxford: Blackwell Scientific Publications, 1993.
25. Heil W, Koberstein R, Zawla B. Reference ranges for adults and children pre-analytical consideration: Boehringer Mannheim, 1997.
26. WHO. Prevention and control intestinal parasitic infections. Report of a WHO Expert Committee. In: series Wtr, ed. Technical Report Series, No. 749. Geneva: World Health Organization, 1987.
27. Dean AG, Dean JA, Coulombier D, Brendel KA, Smith DC, Burton AH, Dicker RC, Sullivan K, Fagan RF, Arner TG. Epi info version 6: a World - processing, database and statistics program for public health on IBM-Compatible Microcomputer. Atlanta: Center for Disease Control and Prevention 1995.
28. Field A. Discovering Statistics using SPSS for Windows. London. Thousand Oaks. New Delhi: SAGE Publications, 2000.
29. FAO, WHO, UNU. Energy and protein requirements. Report of a joint FAO/ WHO/UNU expert consultation. Geneva: World Health Organization, 1985.
30. WHO/FAO/AEA. Trace elements in human nutrition and health. Geneva: World Health organization, 1996.
31. Dung V, Tuan T, Thach T, Ninh N, Boy E, Cervinskas J. Cost-effectiveness of an iron supplementation program for women and children in a rural district of Vietnam. Poster presentation Theme 33, INACG Symposium, Marrakech, Morocco. 2003.
32. Lipschitz D, Cook JD, Finch C. Clinical evaluation of serum ferritin as an index of iron stores. N Engl J Med. 1974;290:1213-16.
33. Punnonen K, Irjala K. Serum transferrin receptor and its ratio to serum ferritin in the diagnosis of iron deficiency. Blood. 1997;89:1052-7.
34. Broek N van den. Anemia in pregnancy: studies on screening, prevalence and aetiology from South Malawi. PhD dissertation. University of Amsterdam 1998.
35. Ritchie B, Mcneil Y, Brewster D. Soluble transferrin receptor in Aboriginal children with a high prevalence of iron deficiency and infection. Trop Med Int Health. 2004;9:96-105.
36. Kuvibidila S, Warrier R, Ode D, Yu L. Serum transferrin receptor concentrations in women with mild malnutrition. Am J Clin Nutr. 1996;63:596-601.
37. Zhu Y, Haas J. Response of serum transferrin receptor to iron supplementation in iron - deplete, nonanemic women. Am J Clin Nutr. 1998;67:271-275.
38. WHO. Iron deficiency anemia: Assessment, prevention and control. Geneva: World Health Organization, 2000.
39. Kling P, Roberts R, Widness J. Plasma transferrin receptor levels and indices of erythropoiesis and iron status in healthy term infants. J Pediatr Hematol Oncol. 1998;20:309-14.
40. Zimmermann MB, Molinari L, Staubli-Asobayire F, Hess SY, Chaouki N, Adou P, Hurrell RF. Serum transferrin receptor and zinc protoporphyrin as indicators of iron status in African children. Am J Clin Nutr. 2005;81:615-23.
41. Malope BI, MacPhail AP, Alberts M, Hiss DC. The ratio of serum transferrin receptor and serum ferritin in the diagnosis of iron status. Br J Haematol. 2001;115:84-89.
42. Thurlow RA, Winichagoon P, Green T, Wasantwisut E, Pongcharoen T, Bailey KB, Gibson RS. Only a small proportion of anemia in northeast Thai schoolchildren is associated with iron deficiency. Am J Clin Nutr. 2005;82:380-7.
43. Baggett HC, Parkinson AJ, Muth PT, Gold BD, Gessner BD. Endemic iron deficiency associated with Helicobacter pylori infection among school-aged children in Alaska. Pediatrics. 2006:2005-1129.
44. Le HT, Anemia among schoolchildren in Vietnam: the efficacy of iron fortification. PhD thesis, Wageningen: Wageningen University. 2006.
45. Broek N van den, Letsky E. Etiology of anemia in pregnancy in south Malawi. Am J Clin Nutr. 2000;72:247S-256S.
46. Cardoso M, Ferreira M, Camargo L, Szarfarc S. Anaemia, iron deficiency and malaria in a rural community in Brazilian Amazon. Eur J Clin Nutr. 1994;48:326-332.
47. Phillips R, Pasvol G. Anaemia of Plasmodium falciparum malaria. Baillieres Clin Haematol. 1992;5:315-330.
48. Stoltzfus JR, Michele L, Dreyfuss, Hababuu M, Chwaya, Albonico M. Hookworm control as a strategy to prevent iron deficiency. Nutr Rev. 1997;55:223-232.
49. Stoltzfus R, Chwaya H, Tielsch J, Schulze K, Albonco M, Savioli L. Epidemiology of iron deficiency anemia in Zanzibari school children: the importance of hookworms. Am J Clin Nutr. 1997;65:153-9.
50. Islek I, Kucukoduk S, Cetinkaya F, Gurses N. Effects of ascaris infection on iron absorption in children. Ann Trop Med Parasitol. 1993;87:477-81.
51. Nallam N, Paul I, Gnanamani G. Anemia and hypoalbuminia as an adjunct to soil-transmitted helminthiasis among slum school children in Visakhapatnam, South India. Asia Pacific J Clin Nutr. 1998;7:164-169.
52. Faulkner H, Turner J, Kamgno J, Pion S, Boussinesq M, Bradley J. Age- and infection intensity - Dependent Cytokine and antibody production in human Trichuriasis: The importance of IgE. J Infect Dis. 2002;185:665-72.
53. Looker A, Dallman P, Carroll M, Gunter E, Johnson C. Prevalence of iron deficiency in the United States. JAMA. 1997;277:973-6.
54. Tomkins A. Environment, season and infection. Cambridge: Cambridge University press 2005.

Original Article

Anemia and intestinal parasite infection in school children in rural Vietnam

Huong Thi Le PhD[1,2], Inge D Brouwer PhD[2], Hans Verhoef PhD[3], Khan Cong Nguyen PhD[4] and Frans J Kok PhD[2]

[1]*The Nutrition Department, Hanoi Medical University, Vietnam*
[2]*The Division of Human Nutrition, Wageningen University, Netherlands*
[3]*Cell Biology and Immunology Group, Wageningen University, Netherlands*
[4]*The National Institute of Nutrition, Hanoi, Vietnam*

越南鄉村學童貧血及腸道寄生蟲感染

目的：本研究假設除了鐵缺乏之外，腸道寄生蟲感染也是越南鄉村學童貧血的決定因素。**方法**：從越南貧窮的鄉村地區 Tam Nong 省的 20 所國小學童的學籍資料隨機選取 400 名。這個橫斷性研究收集靜脈血(5 毫升)，分析血紅素(Hb)、血清鐵蛋白(SF)、血清運鐵蛋白接受器(TfR)、血清 C-反應蛋白以及總免疫球蛋白 E(IgE)。糞便樣本用來評估鉤蟲、鞭蟲以及蛔蟲感染。使用羅吉斯迴歸評估腸道寄生蟲對貧血的效應。**結果**：貧血盛行率為 25%(Hb<115g/L)，2%的兒童鐵缺乏(TfR >8.5mg/L)。腸道寄生蟲盛行率為 92%，鞭蟲(76%)與蛔蟲(71%)的盛行率較高。超過 30%及 80%的學童其 CRP(≥ 8mg/L)及 IgE(> 90 IU/mL)濃度較高。貧血狀況與 SF 呈邊緣顯著相關，與 TfR 及 CRP 則沒有相關。鞭蟲感染與表現鐵缺乏的 TfR 及 SF 的盛行率勝算比分別為 1.96(95% CI 1.07-3.59)及 2.00(95% CI 1.08-3.65)。**結論**：越南學童的貧血盛行率高，但是與鐵缺乏可能無關。不是因為缺鐵，鞭蟲感染者有兩倍的機會貧血。慢性感染可能是貧血的重要原因，但是仍需要更進一步的研究。

關鍵字：鐵缺乏、貧血、寄生蟲、兒童、越南。