Prevalence and risk factors for iron deficiency in Kelantanese pre-school children

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ABSTRACT

Introduction: To determine the prevalence of iron deficiency (ID) and iron deficiency anaemia (IDA) in Kelantanese pre-school children and to identify risk factors that best predict the presence of ID.

Methods: Children (aged eight to 26 months) who attended eight primary health clinics in the district of Kota Bharu, Kelantan, Malaysia, from September to November 1999, were invited to participate in the study. Parents were interviewed for potential risk factors of ID and blood was taken for the analysis of haemoglobin (HB), mean corpuscular volume and serum ferritin (SF) level after obtaining a verbal consent. The possible risk factors for ID were compared between the iron deficient (SF less than 12 microgrammes per litre) and iron sufficient (SF greater than 12 microgrammes per litre) groups using multiple logistic regression.

Results: Among 490 children, 319 (65.1percent, 95 percent confidence interval [CI] 60.7-69.2 percent) had anaemia (HB less than 11.0 g/dL). 191 children (38.9 percent, 95 percent CI 34.7-43.5 percent) had ID. 155 children (31.6 percent, 95 percent CI 27.6-36.0 percent) had IDA (HB less than 11.0 g/dL and SF less than 12 microgrammes per litre). Independent risk factors for ID were prolonged breast feeding for more than six months (p-value is 0.003, adjusted odds ratio [OR] 2.5, 95 percent CI 1.5-4.0) and failure to receive formula milk (p-value is 0.004, adjusted OR 1.6, 95 percent CI 1.2-2.0). Other dietary factors were not significantly associated with ID.

Conclusion: The prevalence of ID and IDA among Kelantanese children is high, and is mainly attributed to prolonged breast feeding beyond six months of age and failure to introduce formula milk at later infancy.

Keywords: anaemia, iron deficiency, iron deficiency anaemia, pre-school children

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INTRODUCTION

Anaemia is a common problem in childhood, especially in children aged six to 24 months old. It has been estimated that among children below four years of age, 12% are anaemic in developed countries and 51% are anaemic in developing countries[1]. Iron deficiency anaemia (IDA) is the most commonly recognised form of nutritional deficiency in developing[2] and developed countries[3]. About 600 million individuals worldwide have IDA[1] which in most cases, is of dietary origin, such as inadequate weaning[3]. IDA can no longer be considered a simple anaemia that can be readily reversed by iron therapy. Iron deficiency (ID) may be associated with abnormalities in cell-mediated immunity and the ability of neutrophils to kill several types of bacteria[4], and poorer psychomotor development and behavioural changes of young children[5]. Children who have IDA in infancy are at risk for long-lasting developmental disadvantages[6], as well as behavioural and developmental disturbances[7], compared with their peers with a better iron status.

Iron is necessary for maintaining normal structure and function of virtually all mammalian cells, and is also involved in the immune and non-immune host defence. In-vitro studies have shown that iron and iron-binding proteins are important for lymphocyte proliferation, satisfactory functioning of natural killer cells, B cells and antibody production and the activity of phagocytic cells[8]. Thus, it has been suggested that infants and toddlers should be screened for ID. Screening for anaemia, conducted mostly in Western countries, has detected a higher prevalence of ID among Asian children[9,10]. Similar studies for ID and IDA are lacking in our population. This study was designed to determine the prevalence of ID and IDA in Kelantanese pre-school children

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and to identify risk factors that best predict the presence of ID.

METHODS

A cross-sectional survey was conducted from September to November 1999 in eight primary health clinics (Pengkalan Chepa, Kubang Kerian, Perol, Badang, Wakaf Che Yeh, Peringat, Baung Bayam and Ketereh) in the district of Kota Bharu, Kelantan, Malaysia. There were ten primary healthcare clinics in the district of Kota Bharu. Five clinics (Pengkalan Chepa, Kubang Kerian, Perol, Badang and Wakaf Che Yeh) that were geographically representative of the district of Kota Bharu were initially selected for the study. However, because of poor attendance at Perol Clinic, three additional clinics (Peringat, Baung Bayam and Ketereh Clinics) were selected, based on their geograpical locations within the district of Kota Bharu, and visits to the Perol clinic were discontinued.

Children (aged eight to 26 months) who visited the clinics for routine immunisation or routine healthcare follow-up were invited to participate in the study. Children were excluded from the study if they (a) were accompanied by caregivers other than their parents; (b) had an acute infection at the time of the visit; (c) had a history of concurrent chronic illnesses, such as chronic neurological diseases, cyanotic heart disease, chronic liver or renal diseases; and/or (d) had a diagnosis of thalassaemia. Following a verbal consent, information on demographical data and risk factors for ID were obtained from parents, and venous blood was taken from the children.

Blood was drawn from the dorsal venous plexus on the dorsum of the hand using a 22 or 23 gauge needle. About 1 ml of blood was collected into an ethylenediaminetetraacetic acid (EDTA)-coated tube for the full blood count analysis, and a plain tube for the estimation of serum ferritin (SF). Blood samples were taken within four hours of blood collection to the Universiti Sains Malaysia Hospital, Kubang Kerian for analysis. The Coulter counter machine (model JT August 1988 Coulter Electronics Inc, Miami, FL, USA) was used for the measurement of haemoglobin (HB), erythrocyte count and mean red cell volume. The mean corpuscular volume (MCV) was derived from these values. SF was measured using microparticle enzyme immunoassay (MEIA) method on the IMx Analyzer machine (Abbott Laboratories, Abbott Park, IL, USA).

Anaemia was defined as a HB of <11.0 g/dL while ID was defined as SF <12.0 µg/L. Children were classified as having IDA according to several definitions to enable comparison with prevalence in other countries. Among the definitions for IDA used in the literature included: (a) HB<11.0 g/dL and SF<12 µg/L; (b) HB<11.0 g/dL and MCV<70 fL; (c) HB<11.0 g/dL and [MCV<70 fL or SF<12 µg/L]; and (d) HB<11.0 g/dL and [MCV<70 fL and SF<12 µg/L]. The study was approved by the Research and Ethics Committee, School of Medical Sciences, Universiti Sains Malaysia, and Director of Health Services, Kelantan, Malaysia.

Assuming a 30% prevalence of IDA in the population, a sample size of 500 would be required to be 95% certain in estimating an overall prevalence in the sample within ±4% of its true value. Multivariate analysis of risk factors for ID (SF<12 µg/L) were examined using logistic regression for survey data (STATA version 7 for personal computers). The odds ratios (OR), both adjusted and unadjusted, and their 95% confidence intervals (CI) and p-values in these models, were based on the Wald statistics. The presence of interaction was also assessed in the model. All independent variables were entered in the model and the variable with the largest p-value was removed until only variables with p-values ≤0.05 remained.

RESULTS

Among 573 parents interviewed, 83 (14.5%) children were not analysed because of unavailability of consent for venepuncture (46 children), or insufficient collection of blood for estimation of SF (37 children). Among 490 children with complete data, 112 (22.9%) were from Wakaf Che Yeh, 84 (17.1%) from Baung Bayam, 80 (16.3%) from Kubang Kerian, 72 (14.7%) from Badang, 57 (11.6%) from Pengkalan Chepa, 50 (10.2%) from Ketereh, 34 (6.9%) from Peringat and only one (0.2%) from Perol. There were 482 (98.4%) Malays, four (0.8%) Chinese, three (0.6%) Indians and one (0.2%) Thai. The proportion of males (234, 48%) and females (256, 52%) was similar. The ages of children ranged from six to 26 months, with a mean age of 15 months.

319 children (65.1%, 95% CI 60.7-69.2%) had anaemia (HB<11 g/dL). 191 children (38.9%, 95% CI 34.7-43.5%) had ID (SF<12.0 µg/L), and 99 children (20.2%, 95% CI 6.8-24.1%) had both SF<12.0 µg/L and MCV<70 fL. About one-third of the children had IDA (Table I). In the univariate analysis of risk factors for ID (Table II), children who had never been given formula milk (p<0.001, OR 2.2), prolonged breast feeding for more than six months (p=0.001, OR 3.2), housewife mothers (p=0.03, OR 1.5) and low family income (<RM1,000 per month) (p=0.05, OR 1.6) were

significantly associated with ID. Children who had never received breast milk (p=0.04, OR 0.3) were significantly less likely to have ID.

Other factors, including low birth weight, prematurity, late weaning, low protein intake, no vitamin supplementation, history of pica, administration of anti-helminthics during the last six months, delayed immunisation (delay of one month or more in the recommended schedule by the Ministry of Health, Malaysia), gender, low maternal and paternal education (primary school or no education), large family size (more than five children in the family), previous hospital admissions, and low growth parameters (length, weight and head circumference <10th percentile), were not significantly associated with ID. After adjusting for confounders using logistic regression, significant independent risk factors for ID were prolonged breast feeding for more than six months (p=0.003, adjusted OR 2.5, 95% CI 1.5-4.0) and failure to be given formula milk (p=0.004, adjusted OR 1.6, 95% CI 1.2-2.0). There

Table I. Prevalence of iron deficiency anaemia among pre-school Kelantanese children.

Definition of iron deficiency anaemia	Prevalence	
	n	% (95% CI)
HB<11.0 g/dL & SF<12 µg/L	155	31.6 (27.6-36.0)
HB<11.0 g/dL & MCV<70 fL	169	34.5 (30.3-38.9)
HB<11.0 g/dL & MCV<70 fL or SF<12 µg/L	231	47.1 (42.7-51.7)
HB<11.0 g/dL & MCV<70 fL & SF<12 µg/L	93	19.0 (15.7-22.8)

Table II. Risk factors for iron deficiency in Kelantanese pre-school children.

Risk factor	Iron sufficient (SF ≥12.0 µg/L) n=299		Iron deficient (SF <12 µg/L) n=191		p-value	Crude odds-ratio	95% confidence interval
	n	%	n	%			
Low birth weight (<2.5 kg)	26	8.7	21	11.0	0.31	1.3	0.7-2.3
Prematurity (<37 weeks gestation)	9	3.0	6	3.1	0.94	1.0	0.3-4.1
Never breast fed	14	4.7	3	1.6	0.04	0.3	0.1-0.9
Never given formula milk	125	41.8	116	60.7	<0.001	2.2	1.6-2.9
Late weaning (solid food after six months old)	22	7.4	7	3.7	0.31	0.5	0.1-2.3
Prolonged breast feeding (>6 months)	217	72.6	171	89.5	0.001	3.2	2.0-5.1
Low protein intake (meat/chicken/fish <5 times/week)	21	7.0	10	5.2	0.13	0.7	0.5-1.1
No vitamin supplementation during the last six months	138	46.2	87	45.5	0.93	1.0	0.5-1.9
History of pica	80	26.8	54	28.3	0.55	1.1	0.8-1.4
No administration of anti-helminthics during the last 6 months	157	52.5	114	59.7	0.16	1.3	0.9-2 1
Delayed immunisation (≥1 month)	86	28.8	59	30.9	0.79	1.1	0.5-2.6
Female gender	151	50.5	105	55.0	0.46	1.2	0.7-2.1
Low maternal education (primary school or no education)	28	9.4	24	12.6	0.25	1.4	0.7-2.6
Low paternal education (primary school or no education)	26	8.7	22	11.5	0.14	1.4	0.9-2.1
Housewife mothers	227	75.9	157	82.2	0.03	1.5	1.0-2.1
Low family income (<RM1,000 per month)	201	67.2	147	77.0	0.05	1.6	1.0-2.7
Large family size (>5 children)	51	17.1	36	18.8	0.58	1.1	0.7-1.8
Previous hospital admission	22	7.4	11	5.8	0.69	0.8	0.2-3.4
Length <10th percentile	95	31.8	66	34.6	0.65	1.1	0.6-2.1
Weight <10th percentile	86	28.8	69	36.1	0.18	1.4	0.8-2.4
Head circumference <10th percentile	115	38.5	82	42.9	0.43	1.2	0.7-2.0

RM: Malaysian ringgit

was no significant interaction between prolonged breast feeding and failure to give formula milk.

DISCUSSION

The prevalence of ID and IDA varies widely between countries. Depending on the definitions used, between 20.2% (SF<12.0 μg/L and MCV <70 fL) and 38.9% (SF<12.0 μg/L) of children in this study had ID. The prevalence of ID has been shown to be higher in other developing countries, such as South Benin, Africa (62%)[11], Argentina (46%)[12] and Pakistan (67%)[13]. The high prevalence of ID has been attributed to the high prevalence of intestinal parasite infestation, nutritional inadequacy, and the high consumption of pasteurised unfortified cow's milk in these regions. Pasteurised cow's milk is not only a poor source of iron, but its use may also be associated with occult bleeding from the gut. Daly et al found that by 18 months of age, 33% of children consuming cow's milk were anaemic compared with only 2% of those receiving follow-on formulas[14]. Even though 25% of children aged six months to six years in Thailand had anaemia, only 5% of the anaemia was due to ID. It was postulated that the majority of these children who were anaemic could be having thalassaemia or haemoglobinopathes. Asian children (45%) have been shown to have a higher prevalence of ID compared to Caucasian children (23%)[9,15]. This is probably due to the Asian children's consumption of more sweet desserts and less savoury and meat-based foods during their infancy, thus reducing their intake of haem iron. Among the children aged 5 to 14 years in the Aboriginal community in north-west Australia, the high prevalence of ID (78%) and IDA (66%) was attributed to the high prevalence of hookworm infestation (93%)[16].

In this study, ID was significantly associated with prolonged breast feeding for more than six months, and failure to give formula milk. Healthy term infants are born with sufficient iron stores to meet their needs during the first four to six months of life. However, iron stores soon become depleted, and infants who are exclusively breast fed should receive iron supplementation beyond six months of age[17]. Storage iron was shown to be absent in 27.8% of the breast-fed infants versus none of the formula-fed infants at nine months of age[18]. Direct measurements of iron status showed that breast-fed infants developed IDA at six months and that iron reserves were almost exhausted at nine months in most of them as the mean SF value was near the lower limit of the normal range[18]. Breast milk is low in iron (0.2 to 0.4 mg/L) even though the bioavailability of iron is high[19].

Infants breast fed for more than four to six months without receiving iron supplementation or iron–fortified complementary foods are at risk of developing IDA[18,20]. IDA was found to be higher in children who were breast fed for more than six months (28.8%) as compared to those who were formula fed (2.1%)[21]. Iron supplementation from four to nine months, or six to nine months, significantly reduced IDA in Honduran breast-fed infants[22]. During their rapid growth in the first year of life, fortified formulas have been shown to be effective in preventing iron deficiency. Daly et al found only 2% of children on follow-on formula were anaemic at 18 months as compared to 33% on cow's milk, and by 24 months, no children on follow-on formula group was anaemic whereas 26% of children on cow's milk were anaemic. The SF in children on cow's milk was also significantly lower than that in children on follow-on formula[14].

The prevalence of ID, however, is much lower in developed countries, e.g. New York (8%)[23], United States (9%)[24], and European countries (7%)[25]. The lower prevalence of ID in these developed countries is attributed to several factors: improvement in the socio-economic status, avoidance of cow's milk feeding during the first year of life, and improvement in the childhood iron nutrition after the implementation of the special supplemental food programme for women, infants and children (WIC programme)[26]. In this study, 31.6% children had HB <11.0 g/dL and SF <12 μg/L. The prevalence of IDA in other countries varies widely, depending on the definitions of ID. Our result is in concordance with the prevalence of IDA in Argentina (37%)[12] and Cambodian refugees in Dunedin (37%)[27]. The prevalence of IDA in developed countries has been shown to be very much lower, ranging from 2% to 11%. Studies in the United States have reported a considerable decline in the prevalence of ID in early childhood over the past two decades. The decline was attributed to improved feeding practices and preventive programmes[26].

ID causes deficiencies of many iron-dependent enzymes and haem-containing proteins, and is known to produce many systemic abnormalities[17]. ID, with or without concomitant anaemia, can impair growth and intellectual development in children. Epithelial changes in the gastrointestinal tract may lead to angular stomatitis and glossitis. Pica, the compulsive consumption of non-nutritive substances, occurs variably in patients with ID, but the precise pathophysiology of this symptom is unknown. Information on the long-term effects of iron deficiency during infancy highlights the importance of early intervention.

In conclusion, the prevalence of ID and IDA among Kelantanese children is high compared to that in developed countries, and is mainly attributed to prolonged breast feeding beyond six months of age and failure to introduce formula milk during the period of rapid growth in later infancy. Medical personnel, particularly those working in primary health clinics, should have a low threshold for investigating and treating ID, and appropriate dietary advice should be given to prevent this condition. Routine administration of oral iron to babies on prolonged breast feeding may be considered to prevent ID.

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