Cow's milk consumption and childhood anemia in the city of São Paulo, southern Brazil

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Abstract

Objective
To evaluate the influence of the consumption of cow's milk on the risk of anemia during childhood in the city of São Paulo.

Methods
We have studied a probabilistic sample (n=584) of underfive children living in the city of São Paulo, southeastern Brazil, between 1995 and 1996. Anemia (hemoglobin <11g/dl) was diagnosed using capillary blood obtained by fingertip puncture. The cow's milk content and the density of heme and nonheme iron in the child's diet were obtained using 24-hour recall questionnaires. Multiple linear and logistic regression models were used to study the association between cow's milk content in the diet and hemoglobin concentration or risk of anemia, and included statistical control for potential confounders (age, sex, birthweight, presence of intestinal parasites, family income, and mother's schooling).

Results
The prevalence of anemia was 45.2% and the mean contribution of milk to the total caloric content of the children's diets was 22.0%. The association between milk consumption and risk of anemia remained significant, even after considering the dilutive effect of milk consumption on the density of iron in the diet, thus indicating a possible inhibitor effect of milk on the absorption of the iron present in the other foods ingested by the child.

Conclusions
The relative participation of cow's milk in the child's diet showed a significant positive association with risk of anemia in children between ages six and 60 months, regardless of the density of iron in the diet.

INTRODUCTION

Anemia, an insufficient concentration of hemoglobin in blood (<11g/dl), is one of the most frequent nutritional disorders worldwide.[21] Children under age five years are second only to pregnant women in terms of anemia prevalence.[14,21] According to World Health Organization (WHO) estimates, roughly one-half of the underfives in developing countries – China excluded – suffer from anemia. It is estimated that anemia affects 30% of preschool children in Latin America.[14] A probabilistic household survey carried out in the city of São Paulo found a 46.9% prevalence anemia in underfives.[9]

Although a number of factors may lead to anemia, including genetic problems (immunoglobulinopathies, for instance) and parasitic infections (hookworms and other parasites), diets with low iron content or which contain iron with low bioavailability

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are widely acknowledged as the main cause for the high prevalence if this disease in childhood.[13,14,20,21,23]

Diets relying exceedingly on the consumption of cow's milk may be one of the causes of the high risk of anemia observed in the first years of life, since cow's milk is poor in iron (about 2.6 mg Fe per 1,000 kcal). Recommended daily iron consumption between ages six and 60 months is 10 mg, which corresponds to diets with iron densities of 11.7 mg, 7.7 mg, and 5.6 mg for children aged six-11 months, 12-35 months, and 36-60 months, respectively.

In addition to being poor in iron, cow's milk does not contain heme iron, the form which is best absorbed by the body.[3,13] According to experimental data, cow's milk also has the potential to inhibit the absorption of both heme and nonheme iron present in other foods consumed by the child.[4,5,17]

Notwithstanding, the association between the consumption of cow's milk and hemoglobin concentration has been little explored in epidemiological studies. A recent pioneer study using a cohort of European children showed that the hemoglobin concentration reached by children at age 12 months was inversely related to the number of months during which the child consumed cow's milk.[7]

The present study was designed to study the influence of cow's milk consumption on hemoglobin concentrations and on the risk of anemia in underfives.

METHODS

The data used were generated by a survey conducted by the *Núcleo de Pesquisas Epidemiológicas em Nutrição e Saúde da Universidade de São Paulo* (Center for Epidemiological Research in Nutrition and Health, University of São Paulo – NUPENS/USP), between September 1995 and September 1996, based on a probabilistic sample composed of 4,560 households in the city of São Paulo. This survey is known as the *Saúde e Nutrição das Crianças de São Paulo* (Health and Nutrition in São Paulo Children) survey. [8] Sampling was stratified and in multiple stages, involving the random selection of census sectors, household clusters, and individual households. Visits to the 4,560 selected households identified 1,390 children under age five years. Of these, 110 were not included in the survey – either because they were not found after three visits or because parents did not authorize participation – resulting in a total of 1,280 children aged between zero and 59 months. Dietary recalls investigating food consumption in the last 24 hours were administered to all children aged between six and 23 months, and to one of every three children aged between 24 and 59 months, totalling 598 children whose food consumption information are described in the present study. Hemoglobin dosage could not be performed on 14 children, and hence the analyses of the relationship between food consumption and hemoglobin concentration refer to 584 children.

Information on food consumption was provided by the parent or caretaker by a 24-hour dietary recall.[22] Blood samples were obtained by fingertip puncture, and hemoglobin was measured at the child's home using a portable hemoglobinometer (HemoCue®)[19]. The information on salaries and other sources of income and on maternal schooling used in the present study were obtained by questionnaires. Information on the occurrence of intestinal parasitic diseases was obtained from stool samples collected at the child's home and analysed by sedimentation. The child's birthweight was obtained from maternity files, or, alternatively, from information provided by the child's mother.

The level of cow's milk consumption of each child was expressed as the percentage of the child's daily calorie intake which was due to the consumption of any type of milk (whole-milk or modified formula and natural, pasteurized, or long-life fluid milk). The transformation of the foods reported in the 24-hour recall into energy and nutrients was done using *Virtual Nutri*® software.*

As a description of the study population, we present the distribution of hemoglobin concentration, anemia prevalence, and food consumption indicators according to sociodemographic variables. The association with sex was evaluated by Student's *t* and chi-squared tests. Associations with age (6-11, 12-23, 24-35, 36-47, and 48-60 months), per capita family income (0.0 ⊢ 0.5, 0.5 ⊢ 1.0, 1.0 ⊢ 2.0, ≥2.0 minimum wages) and mother's schooling (0-3, 4-7, 8-10, ≥11 years) was evaluated by simple linear regression and chi-squared and linear trend tests.

The influence exerted by the consumption of cow's milk on the iron density in the diet was studied by comparing the observed value with the expected concentration if milk were excluded and substituted by the remaining food items present in the child's diet.

The global effect of the consumption of cow's milk

on hemoglobin concentration was determined based on a multiple regression model in which hemoglobin concentration was the dependent variable and the relative consumption of cow's milk the explanatory variable. Multiple logistic regression was used to evaluate influence over the risk of anemia, with the child's anemia status (absent or present) as the outcome and the terciles of relative milk consumption, expressed as the percentage contribution of milk to the total calorie content of the diet, as the explanatory variable. Child's birthweight, age, and sex, presence of intestinal parasitic disease, per capita family income, and mother's schooling were considered as potential confounders in the association between milk consumption and hemoglobin concentration or anemia. Child's age and sex, per capita family income, and mother's schooling were significantly associated with hemoglobin concentration and/or risk of anemia in simple regression models (p<0.05) and were included in the multiple regression analysis. When measuring the specific effect of milk consumption on hemoglobin concentration – which would be independent of the 'diluting effect' of milk on the density of iron in the diet – heme- and nonheme-iron densities were added to the regression models.

In all analyses, weighting factors were employed in order to allow for the extrapolation of the results obtained in the present study to the entire child population of the city of São Paulo between ages six and 59 months. The α=5% significance level was adopted. All analyses presented in the present study were performed using STATA 6.0 software.

RESULTS

Table 1 presents the distribution of hemoglobin concentration and anemia in the child population of São Paulo according to sociodemographic variables. Anemia was present in 45.2% of children, and was significantly more prevalent among boys than among girls. Anemia prevalence varies strongly with age, peaking at some point between ages six and 12 months and declining slightly in the second year of life and more sharply in the third year. Increases in both per capita family income and mother's schooling were significantly associated with reductions in the prevalence of anemia. Mean hemoglobin concentration is significantly higher in girls than in boys, and tends to increase both with age and with family income and mother's schooling.

The sociodemographic distribution of the characteristics of the child's diet relevant to the present study is presented in Table 2. The percentage participation of milk in the diet decreases significantly with age, there being no uniform pattern of variation along with family income and mother's schooling. The indicators of iron density in the child's diet increased significantly with age, per capita family income, and mother's schooling, with the exception of nonheme iron, which did not differ significantly between the groups. There were no significant differences between sexes with respect to milk consumption or iron density indicators.

The mean iron density in the milk consumed by the studied children (2.7 mg/1000 kcal) was lower than

Table 1 – Distribution of hemoglobin concentration according to sex, age, and socioeconomic indicators.

Strata	N	Hemoglobin (g/dl) $\overline{x}$	(sd)	%<11.0
Sex				
Male	313	10.8**	(1.95)	49.8*
Female	271	11.3	(1.98)	39.8
Age (months)				
6-11	131	10.2****	(1.72)	71.7****
12-23	255	10.4	(1.76)	63.5
24-35	74	10.9	(1.55)	49.3
36-47	61	11.8	(1.64)	29.3
48-60	63	11.6	(1.35)	23.1
Per capita family income (Brazilian minimum wages. Oct/1996)				
0.0 ⊢ 0.5	57	10.6****	(2.04)	52.8****
0.5 ⊢ 1.0	160	10.8	(2.15)	53.7
1.0 ⊢ .0	181	11.0	(2.02)	43.7
≥2.0	186	11.3	(1.77)	38.2
Mother's schooling (years)				
0-3	92	10.9****	(2.59)	42.0***
4-7	239	10.9	(2.01)	48.3
8-10	122	10.9	(1.88)	53.2
11 +	131	11.5	(1.60)	34.7
Total	584	11.0	(1.93)	45.2

N: Number of observations; $\overline{x}$: mean; sd: standard deviation
*p<0.05
**p<0.001
***p for linear trend <0.05
****p for linear trend <0.001

Table 2 – Percentage of calories derived from milk and iron density in the diet according to sex, age, and socioeconomic indicators.

Strata	% calories form milk $\overline{x}$ (sd)	Iron density (mg/1,000 kcal) Total $\overline{x}$ (sd)	Heme $\overline{x}$ (sd)	Nonheme $\overline{x}$ (sd)
Sex				
Male (N=319)	22.0 (18.22)	5.5 (2.50)	1.1 (1.61)	4.4 (2.32)
Female (N=279)	21.9 (16.2)	5.3 (2.51)	1.1 (1.50)	4.2 (2.17)
Age (months)				
6-11 (N=135)	31.7 (19.64)**	5.0 (2.67)*	0.6 (0.93)**	4.4 (2.44)
12-23 (N=259)	26.9 (17.22)	5.4 (2.25)	1.0 (1.13)	4.4 (2.25)
24-35 (N=78)	21.8 (15.10)	5.4 (2.03)	1.2 (1.41)	4.2 (1.59)
36-47 (N=63)	20.6 (11.51)	5.6 (2.22)	1.2 (1.19)	4.4 (2.14)
48-60 (N=63)	13.1 (10.64)	5.5 (1.82)	1.4 (1.27)	4.1 (1.59)
Per capita family income (Brazilian minimum wages. Oct/1996)				
0.0 ⊢ 0.5 (N=58)	22.1 (17.21)	5.4 (2.97)*	0.7 (1.22)*	4.7 (3.05)*
0.5 ⊢ 1.0 (N=160)	22.5 (18.97)	5.5 (2.40)	1.2 (1.77)	4.3 (2.15)
1.0 ⊢ 2.0 (N=189)	21.8 (17.60)	5.4 (2.48)	1.2 (1.79)	4.2 (1.79)
≥2.0 (N=191)	21.7 (16.03)	5.4 (2.49)	1.1 (1.11)	4.3 (2.49)
Mother's schooling (years)				
0-3 (N=94)	21.0 (19.00)	5.3 (2.62)**	1.2 (1.84)*	4.1 (1.94)**
4-7 (N=245)	21.7 (18.62)	5.3 (2.50)	1.0 (1.57)	4.3 (2.35)
8-10 (N=126)	24.8 (14.93)	5.4 (2.36)	1.2 (1.68)	4.2 (2.13)
11 or + (N=133)	20.5 (15.80)	5.5 (2.42)	1.1 (1.27)	4.4 (2.31)
Total (N=598)	22.0 (17.36)	5.4 (2.45)	1.1 (1.47)	4.3 (2.20)

N: number of observations; $\overline{x}$: mean; sd: standard deviation
*p for linear trend <0.05
**p for liner trend <0.001

the mean iron density in the children's diets (5.40 mg/1000 kcal). The 'diluting effect' of milk on the iron density of the diet was estimated at 22%. This value was obtained by comparing the iron density observed in the diet with the estimated density in case milk were suppressed from the child's diet (5.40 mg/1000 kcal in the first scenario vs. 6.17 mg/1000 kcal in the second).

Table 3 presents the results of linear regression between cow's milk consumption and hemoglobin concentration. The percentage of the total daily calories ascribed to milk was significantly correlated with the children's hemoglobin concentration . However, this correlation was not independent of the density of heme and nonheme iron in the diet. Note that the standardized regression coefficient between milk consumption and hemoglobin concentration was only

slightly altered after controlling for the indicators of iron density in the diet. The result of controlled Model C (0.0822) is quite similar to that of non-controlled Model B (0.1048). This indicates that the negative effect of milk consumption on hemoglobin concentration via an inhibition of iron absorption should not be disregarded.

Table 4 presents the results of logistic regression models of the association between terciles of relative milk consumption and risk of anemia. Positive associations between these variables were obtained both in Model B (adjusted only for sex, age, and socioeconomic variables), and in Model C (adjusted also for the iron density of the diet). Model B shows that the odds ratio for anemia increased by about 50% and 100% when children with intermediate (2nd tercile)

Table 3 – Standardized regression coefficients for the association between relative milk consumption and (% of total calories derived from milk) and hemoglobin concentration in three linear regression models.

Model	Adjustment variables	Regression coefficient (ß)	P
A	None	-0.2435	0.000
B	Sex, age, mother's schooling, and log per capita family income	-0.1048	0.031
C	Variables in model B plus density of heme and nonheme iron in the diet	-0.0822	0.081

Table 4 – Prevalence of anemia (hemoglobin <11 g/dl) according to terciles of relative milk consumption and corresponding crude and adjusted odds ratios (OR).

Relative milk consumption (%total daily calories derived from milk)	Prevalence of anemia	Crude OR	Adjusted OR OR	Model B 95%CI	p	OR	Model C 95%CI	P
					0.010			0.041
1st Tercile	35.44	1.00	1.00			1.00		
2nd Tercile	44.86	1.48	1.45	[0.85;2.45]		1.40	[0.81;2.42]	
3rd Tercile	56.39	2.35	2.03	[1.18;3.49]		1.87	[1.06;3.28]	

CI: confidence interval
Model B: ORs adjusted for age group and child's sex, log per capita family income, and mother's schooling.
Model C: ORs adjusted for the variables in model B plus density of heme and nonheme iron in the diet.

or high (3rd tercile) milk consumption, respectively, are compared with children with low milk consumption (1st tercile). Controlling for variations in the iron density of the diet has little effect on the excess risk of anemia among children with higher milk consumption, which reinforces the relevance of the mechanism of inhibition of iron absorption associated with the consumption of cow's milk.

DISCUSSION

In the present study we have shown that increases in the relative participation of cow's milk in the child's diet are associated significantly and independently with increased risk of anemia. This was based on a representative sample of the children living in the city of São Paulo aged between six and 59 months, and on the collection and analysis of information on the consumption of cow's milk, hemoglobin concentration, and potential confounders. The association between milk consumption and risk of anemia remained significant even after considering the dilutive effect of milk consumption on the iron density of the diet, thus indicating a possible inhibitive effect of milk on the absorption of the iron present in other foods in the child's diet.

Although we acknowledged that the instruments used for measuring food consumption (recall questionnaire) and hemoglobin dosage (portable hemoglobinometer) may leave room for measurement errors,[10,22] such errors are probably not associated, therefore leading to an underestimation of the magnitude of the actual association between milk consumption and anemia. It is also important to note that the evaluation of the child's food consumption took place before the measurement of hemoglobin concentration. Thus both the interviewer and the mother were unaware of child's anemia status at the time the questionnaire was administered, reducing the risk of systematic errors.

The probabilistic character and the successful implementation of the procedures employed for selecting the original sample of the *Saúde e Nutrição das Crianças de São Paulo* survey indicate that the results of the present study may be extended to the entire child population of the city of São Paulo.

Likewise, the magnitude and distribution of anemia, and the child feeding patterns in the city of São Paulo are similar to those found in other Brazilian urban centers, which could favor a greater generalization of the results obtained in the present study. A probabilistic household survey conducted in the city of Salvador, northeastern Brazil, in 1996, found a 46.4% prevalence of anemia among underfives, a level similar to

the 45.2% found in São Paulo.[6,9] Still in the city of Salvador, where food consumption in the last 24 hours was also studied, the iron density in the diet was 5.6 mg/1,000 kcal in the six to 11 months age group and 5.8 mg/1,000 kcal in the 12 to 23 months age group. Again, these values were similar to those found in São Paulo, 5.0 mg/1,000 kcal and 5.4/1,000 kcal in these two age groups, respectively. An important participation of milk in the diet was also observed in Salvador, where the participation of milk in the total calorie value was 36.7% in the six to 11 months age group and 31.9% in the 12 to 23 months group. The corresponding values in São Paulo were 31.7% and 26.9% in these two age groups, respectively.[11]

Three other probabilistic surveys conducted in the 1990's in urban centers in the Northeast and South Regions of Brazil showed prevalences of anemia in childhood very close to the 45.2% found in the present study: 39.6% in the metropolitan area of Recife, Northeast Region, in 1997,[16] 47.8% in Porto Alegre, South Region, in 1997 (children under age three years),[18] and 54.0% in Criciúma, also in the South Region, in 1996 (children under age three years).[12] The age distribution of the prevalence of anemia – peaking in the six to 24 month period and falling in older age groups – observed in the São Paulo study was also found in the above mentioned studies.

Theoretically, the negative influence of milk consumption on the hemoglobin concentration may be due to two mechanisms: dilution and inhibition. The dilution mechanism is related to the low concentration of iron present in cow's milk, whereas the inhibition mechanism is related to the presence, in cow's milk, of substances such as calcium, casein, and serum proteins, which are proven inhibitors of iron absorption by the human organism.[4,5,17] Our results confirm the importance of both mechanisms.

Another potential mechanism for the negative influence of cow's milk on hemoglobin concentration is the appearance of micro-hemorrhages in the intestinal mucosa, which would be induced by the consumption of natural or pasteurized milk, but not by diluted formula. Such micro-hemorrhages have been reported in the literature, particularly among infants.[1,15] However, the inclusion, in our regression models, of the type of milk ingested by the child did not indicate an association between this variable and hemoglobin concentration, neither in the whole underfive sample, nor among infants only (data not shown).

It is important to note that the excessive consumption of non-modified cow's milk is not usually mentioned as a relevant determinant of childhood anemia

in national or international publications on the subject.[2,11,20,21] A recent WHO publication, however, recommends that the ingestion of milk not coincide with the child's major meals.[23]

As mentioned above, due to the low precision of the instruments used for measuring food consumption and hemoglobin concentration, the impact of milk consumption on the risk of childhood anemia is likely to be higher than that observed. More precise regression models – based on the refinement of food consumption and hemoglobin concentration measurement and possibly including the time intervals between major meals and milk consumption – would be required in order to better evaluate the potential of orientations aimed at reducing (and/or better distributing throughout the day) the relative consumption of milk to control anemia during childhood.

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