Association between anemia and subclinical infection in children in Paraíba State, Brazil

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Background*: With subclinical infection, serum iron concentrations are reduced, altering the synthesis of hemoglobin, the main indicator of anemia.*

Objective*: To evaluate the association between subclinical infection and anemia in children of Paraíba State.*

Methods*: This is a cross-sectional study involving 1116 children aged 6 to 59 months from nine municipalities of Paraíba State. Demographic and socioeconomic data were collected by means of a specific questionnaire. The C-reactive protein and hemoglobin levels were determined by the latex agglutination technique and automated counter, respectively. C-reactive protein values ≥ 6 mg/L were used as indicative of subclinical infection, while the presence of anemia was determined by hemoglobin values < 11.0 g/dL. The data were analyzed using the Epi Info computer program, with significance being set at 5%.*

Results: *Data from this research showed that 80.1% of the children belonged to families that were below the bread line, with per capita income < ½ of the minimum wage at that time (R$ 350.00 - approximately US$ 175.00). The prevalences of subclinical infection and anemia were 11.3% and 36.3%, respectively. Subclinical infection was significantly associated with anemia (p-value < 0.05). There were lower levels of hemoglobin in children with C-reactive protein ≥ 6 mg/L, with a mean hemoglobin level in children with subclinical infection of 10.93 g/dL (standard deviation - SD = 1.21 g/dL) and without infection of 11.26 g/dL (SD = 1.18 g/dL) (p-value < 0.05).*

Conclusion: *Anemia is associated with subclinical infection in this population, indicating that this is an important variable to be considered in studies of the prevalence of anemia in children.*

Keywords: *Infection; Hemoglobin; Anemia; Child; Public health*

Introduction

Anemia remains a serious public health problem at a global scale, especially in developing countries, where it affects a fairly high percentage of biologically vulnerable groups such as children. Iron deficiency has been identified as the most common cause of anemia but the proportions are not fully yet established as they vary depending on age, gender, socioeconomic conditions and the prevalence of other causes of anemia.[1-3]

Iron is an immunomodulating nutrient involved in different processes of humoral and cellular immunity. The range of activities involving this micro-nutrient makes it essential for an integral immune system. Consequently, during infection the demand for this mineral increases, thus aggravating the patient's iron status.[4,5]

During infectious processes, changes in the serum concentrations of certain proteins, the so-called acute phase proteins (APP) including C-reactive protein (CRP), occur.[6,7] The CRP plasma concentration increases rapidly within about 10 hours of the onset of an acute inflammation and so this is an important indicator of subclinical infection.[6]

Moreover, there is a drop in available iron for the synthesis of hemoglobin during infectious processes because of the retention of intracellular iron such as ferritin, and decreased blood transport of iron due to reduced concentrations of the enzyme involved in transporting the mineral (transferrin).[8-10] Thus, changes in the functions of transport and storage are also factors that explain a reduction in the concentrations of iron during infections.[6,8-10] These changes can occur within the first hours of the infectious process.[6]

It is also noteworthy that infectious processes can cause an increased production of hepcidin by hepatocytes, leading the individual to acondition of hypoferremia limiting iron availability for erythropoiesis and contributing to the development of anemia.[11]

Therefore, the presence of even subclinical infection is a variable that may cause an overestimation of iron-deficiency anemia, especially in populations where infection rates are often high. Hence, the impact of infections is greater in children than adults as the child population is more susceptible to infectious diseases. Many studies do not consider the fact that subclinical infections can lead to a misinterpretation of nutritional status and that significant changes in immunological markers can be observed in apparently healthy children.[12]

Although an association between subclinical infection and a deficit in the hemoglobin (Hb) blood concentrations has been established, works on this subject in Brazil are scarce. Thus, the interest in contributing to national data on this issue prompted this study which aimed to evaluate the association between subclinical infection and anemia in children in Paraíba State.

Methods

This study is part of a wider research project developed in Paraíba State in the period from January to April 2007. One of the objectives of this study was to estimate the prevalence of anemia in the state. This cross-sectional study was designed to evaluate the association between subclinical infections, determined by CRP levels and Hb concentrations in 6 to 59-month-old children.

The children were randomly selected according to multiple-step sampling. For this selection, the populations of the municipalities of the state were estimated from the data published by the Brazilian Institute of Geography and Statistics (IBGE) for 2006. Subsequently, we carried out a survey of the number of 6 to 59-month-old children (15% of the population) with their accumulated populations living in urban areas. After calculating the sampling interval, we proceeded to randomize the municipalities, the census tract, households and children. Nine towns were randomly included in the study: Conceição, Belém do Brejo do Cruz, Boa Ventura, Pedra Branca, São José de Espinharas, Malta, Patos, João Pessoa and Campina Grande.

The population of the original project consisted of 1211 children. Of these, only children with data on the CRP and Hb were included in this study. Additionally, only those children whose parents or guardians formally consented by signing written consent forms participated in the study. Chronic clinically-detectable infections (tuberculosis, pneumonia, colds, etc.) and symptoms possibly related to infections such as fever and diarrhea were exclusion criteria. The final sample size was 1116 children.

The demographic and socioeconomic data were taken from the questionnaires filled in by parents or guardians in the original study.

The Hb and CRP concentrations were determined in an automated counter (Sysmex SF - 3000, Roche Diagnostics) and by latex agglutination, respectively using blood samples of the children collected by peripheral venipuncture. Samples were collected in the morning and due to the difficulty of children fasting, not all obeyed this criterion.

The interpretation of Hb followed the classification criteria used for studies on anemia: mild anemia (> 9.0 g/dL and < 11.0 g/dL), moderate anemia (> 7.0 g/dL and < 9.0 g/dL), severe anemia (< 7.0 g/dL) and normal (without anemia) (> 11.0 g/dL). The presence of subclinical infection was characterized by CRP values ≥ 6 mg/L.

Data were entered in duplicate with subsequent evaluation of the consistency using the validate function (Epi Info). They were then analyzed using the Epi Info statistics program version 6.04b. Statistical analysis was performed considering the descriptive level $\alpha = 5\%$.

The project was evaluated and approved by the Research Ethics Committee of the institution (Nº 1128.0.133.000-05) and subject to the guidelines of Resolution 196/96 of the Brazilian National Health Council.

Results

Table 1 shows the demographic and economic profile of the studied sample. Slightly more than half (51.0%) of the children were male. The mean age was 33.4 months old (standard deviation - SD = 15.7 months old); there was no statistically significant difference between genders (p-value > 0.05). Most of the families (80.1%) were below the bread line, with per capita income less than ½ minimum wage at the time (R$ 350.00 – approximately US$ 175.00). The average per capita income was R$ 130.45 (SD = R$ 120.53) with a minimum of R$ 0.00 and a maximum of R$ 1330.00.

A little more than one third of the children (36.3%) had low Hb levels (< 11.0 g/dL) characterizing anemia with 0.4% being severely anemic (Figure 1).

Table 2 demonstrates that there was no significant difference in the Hb levels between genders (p-value = 0.552). However, older children had a higher mean Hb (p-value < 0.001).

Table 1 - Distribution of children according to demographic and socioeconomic characteristics

Variable	n	%
Gender		
Male	569	51.0
Female	547	49.0
Total	1116	100.0
Age (months)		
≥ 6 and < 24	305	32.7
≥ 24 and < 48	486	43.6
≥ 48 and < 49	265	23.7
Total	1116	100.0
Per capita income*		
< ¼ minimum wage	473	42.9
≥ ¼ and ≤ ½ minimum wage	410	37.2
> ½ minimum wage	220	19.9
Total	1103	100.0

*unknown for 13 children; Minimum wage = R$ 350.00 (approximately US$ 175.00)

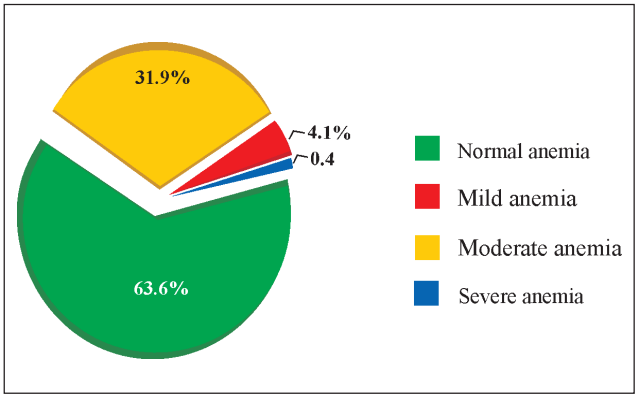

Figure 1– Distribution of children according to hemoglobin levels

Table 2 - Distribution of children according to gender, age and hemoglobin means

Variable	n	%	Hemoglobin (g/dL) Mean (SD)	p-value
Gender				
Male	569	51.0	11.2 (1.2)	0.595
Female	547	49.0	11.2 (1.1)	
Age (months)				
≥ 6 and < 24	365	32.7	10.5 (1.2)	<0.001
≥ 24 and < 48	486	43.6	11.4 (1.1)	
≥ 48 and ≤ 49	265	23.7	11.8 (0.9)	

Infection and anemia

Among the participants, 126 (11.3%) had CRP levels ≥ 6 mg/L suggesting infection while 990 (88.7%) had CRP values within the normal range (CRP < 6 mg/L) (Figure 2).

Table 3 shows that there was a statistically significant association between CRP levels and anemia (p-value = 0.037); the prevalence of anemia in children with elevated CRP levels (45.2%) was significantly higher than in those with normal CRP levels. Thus, children with elevated CRP had significantly lower mean Hb levels (p-value = 0.005 – Table 4).

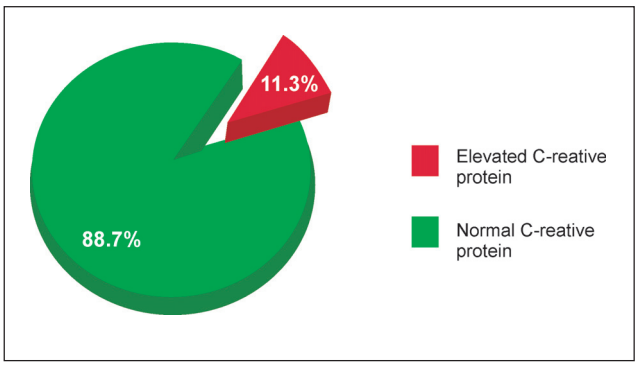

Figure 2 – Percentages of children with normal and high levels of elevated C-reactive protein

Table 3 - Analysis of the association between elevated CRP and anemia

	CRP			
Variable	≥ 6 mg/L n = 126	< 6 mg/L n = 990	χ^2	p-value
Anemia				
Yes	45.2%	35.30%	4.33	0.037
No	54.8%	64.70%		

Table 4 - Means (SD) of hemoglobin according to C-reative protein

	CRP		
Variable Means (SD)	≥ 6 mg/L	< 6 mg/L	p-value
	n = 126	n = 990	
Hemoglobin (g/dL)	10.93 (1.21)	11.25 (1.20)	0.005

Discussion

Iron deficiency is a public health problem in Brazil, especially in the Northeastern region that has large poor areas; this contributes considerably to increase in this nutritional deficiency.[5]

In this study, we observed a prevalence of anemia of 36.3%, a result quite similar to another study conducted in Paraíba in 1992 involving 1287 6- to 59-month-old children that reported a prevalence of 36.4%.[3] These data point to anemia in the state as being a moderate public health problem according to criteria of the World Health Organization.[1]

Similar results were found in two other northeastern states, Pernambuco and Piauí, with prevalences of anemia of 31.8% and 33.8%, respectively.[13,14]

Most of the families (80.1%) had an income per capita of less than half the minimum wage and thus the majority live below the bread line. The low income inhibits access to goods and services, including food, housing and sanitation, essential to maintain the health of family members, hence creating a favorable environment for nutritional deficiencies, infections and infestations.[15]

There was no statistical significance between anemia and gender of the children; these results corroborate studies in Santa Catarina[16] and Minas Gerais.[17]

However, there was a highly significant statistical association between age and Hb concentrations. Hb levels increased with age, a higher prevalence of anemia was observed in young children between the ages of 6 and 24 months old thereby corroborating other Brazilian studies.[16,18,19] This result can be explained by the fact that the period from 12 to 24 months old corresponds to a stage in life during which the growth rate is intense, with an increase in demand for iron.[20] Moreover, it is possible that the anemia in these children manifests in the first year of life, that is during the 6 to 12-month-old period, due to early

weaning and/or delay in the introduction of iron-rich foods.[21] The decrease in the growth rate and the gradual transition from an essentially milk diet to a more varied diet, rich in foods containing iron, contribute to a decrease in the prevalence of anemia in older children.[20]

The results of this study also showed that the prevalence of anemia was significantly higher in the presence of an acute phase response as this reduces serum iron concentrations thereby impairing Hb synthesis. Some authors argue that if an increase in the prevalence of acute phase responses is related to an increased prevalence of iron deficiency, one may expect a reduction in Hb concentrations in this population.[6]

However, the few studies addressing this issue have shown conflicting results. In the present study showed that the plasma concentration of hemoglobin was significantly lower in children with elevated CRP level. The same was not observed in studies conducted in Kenya,[22] Peru[23] and Indonésia,[6] which showed no statistically significant association between hemoglobin and CRP variables.

These findings show that there is a controversy about the association between iron and infections and the scarcity of studies in this area. It is unclear to what extent iron deficiency affects an individual during an infectious process.[24] Although studies show that infectious processes cause a decrease in plasma iron[12] and this mineral is known to be a major constituent of Hb,[10] few studies analyze the direct effects of subclinical infection on Hb concentrations. We still believe it is important to consider the possible influence of social and health conditions on the population.

But in the case of regions with high infection rates, such as socio-economically vulnerable areas of Brazil, it is evident that there is a need to assess the presence of infection, albeit subclinical, in studies on the prevalence of anemia by measuring acute phase proteins. This will help to obtain more concrete data on the prevalence of anemia and its causative factors in the population, which are relevant in developing programs to combat this nutritional deficiency.

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References

1. World Health Organization. Worldwide prevalence of anaemia 1993-2005: WHO global database on anaemia. Geneva, Switzerland: World Health Organization; 2008. 48 p.
2. Batista Filho M, de Souza AI, Bresani CC.[Anemia as a public health problem: the current situation]. Cienc Saúde Coletiva. 2008; 13(6):1917-22. Portuguese.
3. Oliveira RS, Diniz AS, Benigna MJ, Miranda-Silva SM, Lola MM, Gonçalves MC, et al. [Magnitude, geographic distribution and trends of anemia in preschoolers, Brazil]. Rev Saúde Pública. 2002;36(1):26-32. Portuguese.
4. Ekiz C, Agaoglu L, Karakas Z, Gurel N, Yalcin I. The effect of iron deficiency anemia on the function of the immune system. Hematol J. 2005;5(7):579-83.
5. Brasil. Ministério da Saúde. Secretaria de Políticas de Saúde. Política Nacional de Alimentação e Nutrição. Brasília: Ministério da Saúde; 2009.
6. Wieringa FT, Dijkhuizen MA, West CE, Northrop-Clewes CA, Muhilal. Estimation of the effect of the acute phase response on indicators of micronutrients status in Indonesian infants. J Nutr. 2002;132(10):3061-6.
7. Jawetz E, Levinson W. Microbiologia médica e imunologia. 7ª ed. Porto Alegre: Artmed; 2005. 632 p.
8. Bricks LF. Ferro e infecções: Atualização. Pediatria (São Paulo). 1994;16(1):34-43.
9. Thurnham DI. Micronutrients and immune function: some recent developments. J Clin Pathol. 1997;50(11):887-91.
10. Zago MA, Falcão RP, Pasquini R. Hematologia: fundamentos e práticas. São Paulo: Atheneu; 2004.
11. Grotto HZ. Metabolismo do ferro: uma revisão sobre os principais mecanismos envolvidos em sua homeostase. Rev Bras Hematol Hemoter. 2008;30(5):390-7.
12. Thurnham DI, Mburu AS, Mwaniki DL, Wagt A. Micronutrients in childhood and the influence of subclinical inflammation. Proc Nutr Soc. 2005;64(4):502-9.
13. UNICEF/Governo do Estado do Piauí. Crianças e adolescentes no Piauí. Saúde, educação e trabalho. Teresina: Governo do Piauí; 1992.
14. Osório MM, Lira PI, Batista-Filho M, Ashworth A. Prevalence of anemia in children 6-59 months old in the state of Pernambuco, Brazil. Rev Panam Salud Publica. 2001;10(2):101-7.
15. Monteiro CA, Freitas IC. [Evolution of socioeconomic determinants of health in childhood in the city of São Paulo, Brazil (1984-1996)]. Rev Saúde Pública. 2000;34(6):8-12. Portuguese.
16. Neuman NA, Tanaka OY, Szarfarc SC, Guimarães PR, Victora CG. [Prevalence and risk factors for anemia in Southern Brazil]. Rev Saúde Pública. 2000;34(1):56-63. Portuguese.
17. Silva DG, Franceschini SC, Priore SE, Ribeiro SM, Szarfarc SC, Souza SB, et al. Anemia ferropriva em crianças de 6 a 12 meses atendidas na rede pública de saúde do município de Viçosa, Minas Gerais. Rev Nutr. 2002;15(3):301-8.
18. Oliveira MA, Osório MM, Raposo MC. Socioeconomic and dietary risk factors for anemia in children aged 6 to 59 months. J Pediatr (Rio J). 2007;83(1):39-46.
19. Monteiro CA, Szarfarc SC. [Health conditions of children of the municipality of São Paulo, SP (Brazil), 1984-1985. V--Anemia]. Rev Saúde Pública. 1987;21(3):255-60. Portuguese.
20. Brunken GS, Szarfarc SC. Anemia ferropriva em pré-escolares: conseqüências formas de controle e histórico das políticas nacionais de redução da deficiência. Cad Nutr. 1999;17:1-19.
21. Silva LS, Giugliani ER, Aerts DR. [Prevalence and risk factors for anemia among children in Brazil]. Rev Saúde Pública. 2001;35 (1):66-73. Portuguese.
22. Verhoef H, West CE, Ndeto P, Burema J, Beguin Y, Kok FJ. Serum transferrin receptor concentration indicates increased erythropoiesis in Kenyan children with asymptomatic malaria. Am J Clin Nutr. 2001;74(6):767-75. Comment in: Am J Clin Nutr. 2002;76(3): 691-3; author reply 693-4.
23. Brown KH, Lanata CF, Yuen ML, Peerson JM, Butron B, LonnerdalB. Potential magnitude of the misclassification of a population's trace element status due to infection: example from a survey of young Peruvian children. Am J Clin Nutr 1993;58(4):549-54.
24. Gera T, Sachdev HP. Effect of iron supplementation on incidence of infectious illness in children: systematic review. BMJ. 2002; 325(7373):1142. Comment in: J Pediatr. 2003;142(5):588. BMJ. 2002;325(7373):1125.