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Original Research Article

Evaluation of the Etiology of Anemia in Children and the Risk Factors Involved

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Abstract: The aim of the study was to evaluate the various etiologies of anemia in children and determine the significance of various associated factors. This cross-sectional study was conducted among 30 anemic children aged six months to 14 years admitted in a tertiary care hospital. Children with fever and other signs of inflammation were excluded. Hemoglobin, serum iron, ferritin, total iron binding capacity, vitamin B12, folic acid, and reticulocyte count were measured. Details regarding breastfeeding habits, age of weaning, worm infestation, and pica were obtained. In results although 56.7% of the children presented with only iron deficiency, 44.3% presented with other etiologies, such as folate deficiency, vitamin B12 deficiency, hemolytic anemia, and anemia of chronic disease. Breastfeeding, weaning, history of pica and worm infestation did not show any association with the occurrence of iron deficiency anemia. In conclusion Due to the multifactorial etiology of anemia, a thorough evaluation must be carried out before treating the patient. Though anemia is predominantly triggered by iron deficiency, other causes cannot be neglected. Awareness regarding appropriate breastfeeding and weaning practices as well as the effects of pica and worm infestation on iron levels may lower the incidence of iron deficiency anemia in children.
Keywords: childhood anemia; pediatric hematology; etiology; risk factors; iron deficiency; folate deficiency

INTRODUCTION:

The most common global nutritional disorder, anemia affects 1.62 billion people worldwide and has the greatest impaction children below five years (47.4%) [1]. From a study conducted by JIPMER, anemia was found to be the leading cause of morbidity in school aged children [2]. According to the National Family Health Survey for the year 2005-2006, an alarming 78.9% of children in India between the ages of 6-35 months were found to be anemic [3]. Anemia is a serious public health issue which must be addressed with due importance especially due to its effect on the cognitive and physical development of growing children.

The etiology of anemia is multifactorial in origin. It may be caused by blood loss, nutritional deficiencies, immunological defects, genetic manifestations, or may be secondary to chronic disease [4]. Various other factors also influence the incidence of anemia such as whether the child was breast-fed or formula-fed [5], the duration of breast-feeding (both exclusive and complementary) [6], the age at which the child starts weaning [7], as well as the iron content of the foods first introduced [8]. Furthermore, presence of pica and/or worm infestation may also cause or aggravate an already present iron deficiency anemia. [9, 10].

The terms 'iron-deficiency' and 'anemia' have become essentially synonymous with each other due to the significant association between the two entities. Numerous studies have described the effects of iron deficiency extensively but the role of vitamin B12 and folic acid deficiencies as well as other rarer causes of anemia (such as genetic diseases) has been neglected. [11, 12]. A few recent studies have also reported that iron-deficiency was not in fact the predominant etiology among their findings [12, 13]. Hence a non-biased study is necessary to completely evaluate all the possible causes of anemia in children.

Furthermore, anemia is "one of the commonest preventable causes of death in children under 5 years" according to WHO. [14] A thorough assessment of various lifestyle and cultural health risks is essential to bring about awareness and knowledge especially in rural areas. By evaluating the attribution of certain breast-feeding practices, pica, and worm infestation to iron deficiency anemia, parents can be advised

accordingly to prevent either the onset or exacerbation of anemia in their children.

MATERIALS AND METHODS:

This was a prospective study consisting of 30 anemic patients admitted in the pediatric wards of a tertiary care hospital affiliated to Vydehi Institute of Medical Sciences and Research Center, Bangalore, India. Ethical approval was obtained from the Institutional Ethics Committee. Informed written consent was obtained from the patient's parent/guardian before starting any investigations.

Children aged six months to fourteen years were included in the study whose hemoglobin levels were below the WHO cutoff for anemia: for 6-59 months <11g/dl, 5-11 years <11.5g/dl, 12-14 years <12g/dl. Those who were febrile or presented with any inflammatory conditions were excluded. The subjects were examined for pallor, koilonychias, knuckle pigmentation, and neurological changes. Blood samples were collected and serum iron, serum ferritin, total iron binding capacity, serum vitamin B12, serum folate, and reticulocyte count were measured. In the second part of the study, the attending parent/guardian of the patient was inquired in detail regarding breastfeeding practices such as frequency and duration of exclusive breastfeeding and the age at which the child started weaning. History of pica and/or any worm infestation were also noted. The data was analyzed using SPSS software employing proportions and percentages as well as chi-square test.

RESULTS:

Categorized on a basis of age, 40% of the study population was found to be between six months to 59 months, 40% between five and eleven years, and 20% between 12 to 14 years. The average hemoglobin level among the 30 patients was 9.3 g/dl (Figure 1). 56.7% of the children presented with moderate anemia where hemoglobin ranged from 7.0 to 9.9 g/dl. 36.7% and 6.7% suffered from mild (Hb 10.0 to10.9g/dl) and severe anemia (Hb <7.0g/dl) respectively. The severity distribution among the age groups is illustrated in Figure 2.

Table 1: Descriptive Statistics of Biochemical Measurements

Descriptive Statistics						
	N	Minimum	Maximum	Mean	Std. Deviation	Reference Values
Hb	30	6.30	10.90	9.3087	1.31512	-
Iron(ug/dl)	30	10.0	183.0	35.767	32.3501	50-120
Ferritin(ng/ml)	30	2.7	333.5	44.330	74.0728	23.9-336.2
B12(pg/ml)	30	127.0	732.0	336.033	150.7516	180-914
Folate(ng/ml)	30	4	24	9.66	5.339	5-21
Reticulocyte Count (%)	30	0.1	5	1.68	1.335	0.2-1.0
TIBC (ug/dl)	30	107	635	366.70	117.398	250-450

Table 2: Distribution of Etiologies

Etiology/ Deficiency	Frequency	Percent
IDA	17	56.7
Folate	1	3.3
B12	1	3.3
ACD	3	10.0
HA	2	6.7
Thalassemia	1	3.3
IDA+Folate	4	13.3
IDA+B12	1	3.3
Total	30	100.0

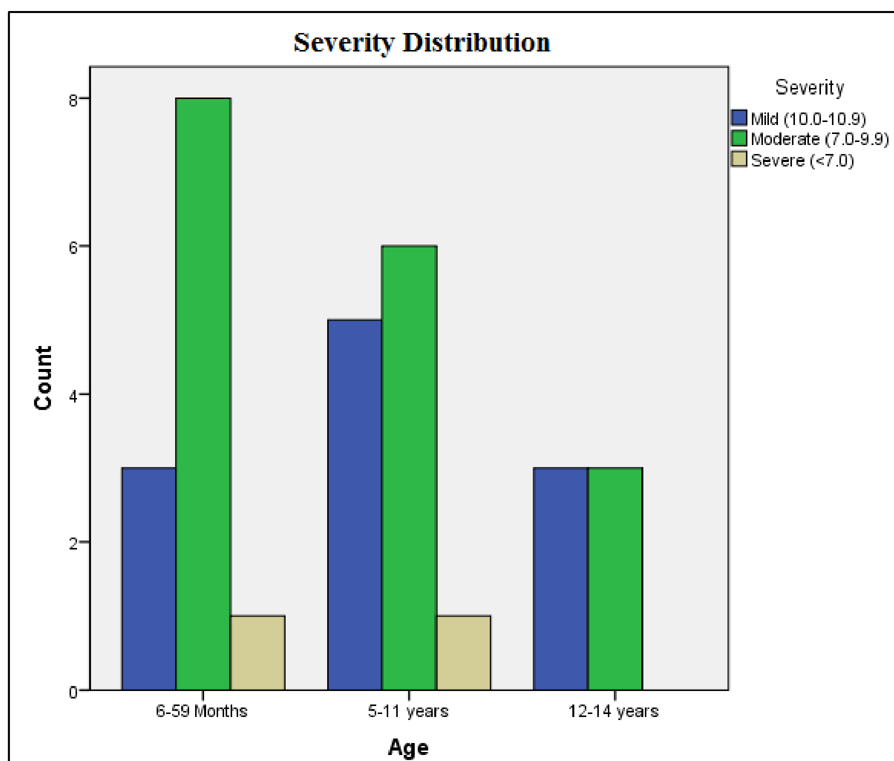

Figure 1: Severity Distribution

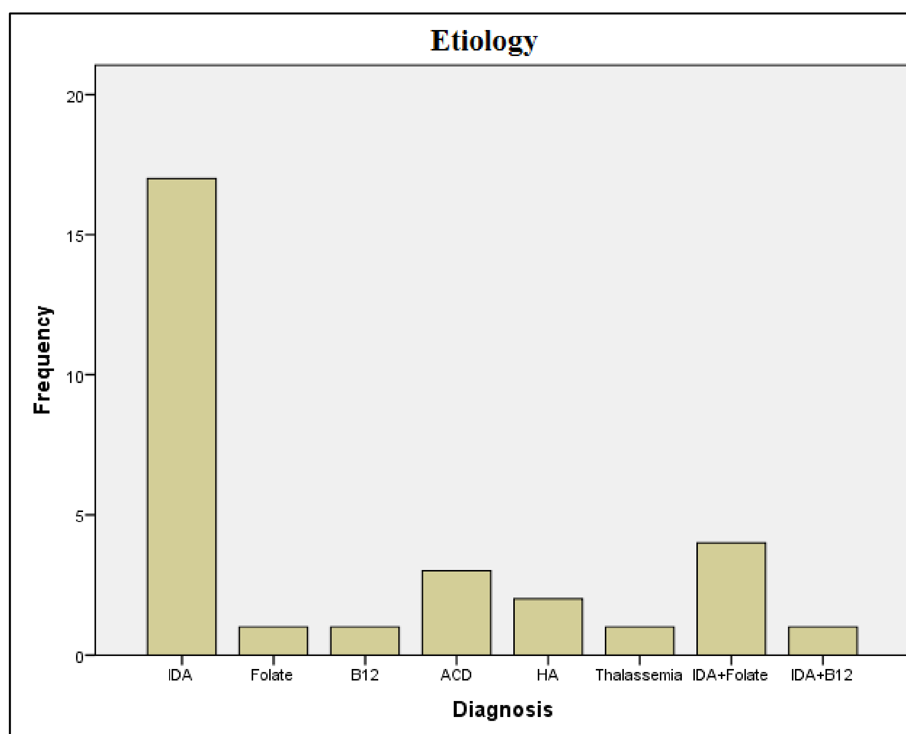

Fig-2: Bar graph showing distribution of etiologies

On clinical examination, 53.3% of children presented with pallor and only two subjects (6.67%) showed any nail changes. None of the patients showed any signs of neurological disturbances.

After biochemical investigation, 56.7% of the patients were diagnosed with iron deficiency anemia, proving to be the predominant etiology in this study. 13.3% of the children showed a mixed deficiency of both iron as well as folate. 10% suffered from anemia

secondary to chronic disease (Figure 3, 4). Other causes such as thalassemia, hemolytic anemias, and anemia due to vitamin B12 deficiency were rare. The highest incidence of iron deficiency was found in the children aged six months to 59 months (83.3% of cases).

Out of the 13 male children, 69.2% were found to be iron deficient whereas out of the 17 girls who took part in the study, a slightly higher fraction (76.5%) presented with iron deficiency. 83.3% of the patients were breastfed at one point in their lives or are currently breastfeeding. Among the 22 children deficient in iron (both pure IDA and mixed etiologies), 18 were breastfed and 4 were formula-fed. However, there was no association found between the incidence of breastfeeding (versus formula feeding) and the occurrence of iron deficiency. 43.3% of the children started weaning around six months of age (five, six, or seven months) out of which 15.4% suffered from an anemia other than IDA. History of worm infestation showed the strongest association to iron deficiency. Out of 17 children who were stated to have history of worm infestation, 13 (76.5%) had presented with iron deficiency. Only 4 subjects claimed to have a history of pica out of which two were diagnosed with IDA and the other two with anemias of other etiology. Chi square test values were not helpful in assessing the relationship between the study parameters due to the small population size.

DISCUSSION:

Anemia is quite common in children especially in developing countries due to the unmet nutritional needs of the growing child. Untreated or misdiagnosed anemia can take a heavy toll on the child's academic performance and general well-being [15]. Iron deficiency is the most widely known cause for anemia. Several studies have reported results similar to those of this study [11, 13, 16-17]. However, many other relevant studies have proven contrary outcomes suggesting that iron deficiency may not be the major reason for pediatric anemia. In an assessment of severe anemia in Malawian children, iron and folate deficiencies were not prominent findings. [18]. A study conducted in Mexico states that anemia not associated with low ferritin levels was found to be more prevalent than iron deficiency anemia[19]. Righty *et al.;* concluded that malaria and chronic inflammation were the most common causes for anemia among infants and school age children respectively in south central Cote d'Ivoire. [20] Hemoglobinopathies and suboptimal vitamin A status were found to be more significant etiologies in a study conducted among northeast Thai school children [21]. In a study conducted by AIIMS, Delhi, vitamin B12 deficiency proved to be the greatest burden among ferritin, folate, and vitamin B12 deficiencies in children aged 5-18 [12]. Hence it is important for pediatricians to diagnose with an unbiased mind when differentiating between various anemias.

The low iron content of breast milk, lack of iron rich complementary food, and the age-related increase in requirement for iron are the main predisposing factors for IDA at a young age [17]. Though the iron in breast milk is said to be more efficiently absorbed by the infant during the first six months of life, formula-fed children had significantly higher hemoglobin concentrations and lower anemia prevalence than breastfed children [5]. For each additional month of breastfeeding after six months, it is calculated that there is a 5% increase in the probability of the child developing IDA. If the child is continued to be exclusively breastfed past one year of age, there is a 1.7 times greater chance of becoming iron deficient [6]. The association between breastfeeding and weaning with IDA in our study was not strong enough to draw any conclusions. However it is advised to avoid cow's milk during the first six months and start weaning with iron containing foods promptly at the age of six months [7]. Recent studies also suggest a supplementation of 1mg/kg/day of oral iron beginning at 4 months of age until fortified complementary foods are started [8].

Pica is a common phenomenon in young children, usually in the form of géophages. Though in this particular study the findings were inconclusive, anemia has been found to be three times more incident in patients with pica than those without pica (highest incidence in children aged four to 15 years) [9]. Contrarily, pica has been described as a consequence of iron deficiency rather than its cause [22].

Parasitic infections, namely hookworm infestations, are significantly associated with anemia in children [10, 20]. Countless studies have been conducted to assess the relationship between various worm infestations in preschool and school going children and iron deficiency anemias. 86.7% were found to be anemic among worm-infested preschool children in tribal Madhya Pradesh [23]. Conversely, 76.8% of school going anemic girls showed evidence of worm infestation in a study conducted in Gulbarga, Karnataka [24]. While chi square tests did not reveal any association, 76.5% of the children with history of worm infestation were found to be iron deficient. This may have been due to the fact that the anemia that developed at the time of the infection has remained unresolved over the years, or it may be due to the subclinical chronicity of the worm infestation manifesting solely as anemia in the individual.

By regulating breastfeeding practices and monitoring for pica and worm infestations, anemia can be controlled to a certain extent without any medical intervention.

CONCLUSION:

While working towards achieving Millennium Development Goal Four, anemia is an important morbidity which must be eliminated. Iron deficiency was found to be the predominant etiology for anemia in this study but it may not always be the case. Therefore a thorough evaluation of the etiology of anemia is essential to accurately administer effective and relevant treatment. It is also the duty of the pediatrician to inform the patient's parent/guardian regarding the recommended breastfeeding and dietary practices to prevent the onset or exacerbation of their ward's anemia. Awareness of pica and worm infestation and its effect on iron deficiency is crucial along with regular deworming.

ABBREVIATIONS:

IDA- Iron Deficiency Anemia
WHO- World Health Organization
JIPMER- Jawaharlal Institute of Postgraduate Medical Education and Research (Puducherry)
AIIMS: All India Institute of Medical Sciences (New Delhi)
ACD- Anemia of Chronic Disease
HA- Hemolytic Anemia

CONFLICT OF INTERESTS:

The authors declare that they have no conflict of interests.

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