American Journal of Public Health Research, 2015, Vol. 3, No. 4A, 57-61
Available online at http://pubs.sciepub.com/ajphr/3/4A/12

DOI:10.12691/ajphr-3-4A-12

Microcytic Hypochromic Anemia in Pediatric Age Group: A Hospital Based Study in Nepal

Arnab Ghosh[1,*], Dilasma Ghartimagar[1], Sushma Thapa[1], Brijesh Sathian[2], Asis De[2]

[1]Department of Pathology, Manipal College of Medical Sciences Pokhara, Nepal
[2]Department of Community Medicine, Manipal College of Medical Sciences Pokhara, Nepal
*Corresponding author: docarnab2k@yahoo.com

Received April 08, 2015; Revised April 29, 2015; Accepted June 26, 2015

Abstract Iron deficiency is a major global health issue and it causes anemia as well as impaired cognitive and motor development and behavioral abnormalities. In developing countries, 39% children below 5 years and 48% children between 5–14 years suffer from anemia. Children with anemia may present in hospital with anemia related nonspecific or specific symptoms or with other associated diseases. In the current study, we have analyzed all pediatric cases with microcytic hypochromic anemia due to iron deficiency. The study was a hospital based retrospective study conducted over a period from September 2013 to December 2014. All cases with age between 1 month to 15 years who had microcytic hypochromic anemia were included in the study and were evaluated for definite diagnoses. All cases with iron deficiency were collated according to age, sex, social status, clinical features and presentation. A total of 422 cases of microcytic hypochromic anemia including 400 cases with iron deficiency were seen in the study period. Male to female ratio was 1.5:1 and the mean age was 4.9 years. The commonest age group was between 1-6 years (45%), followed by the group below 1 year of age (33.8%) and those above 6 years of age (21.2%). The majority of the patients were in the lower socio economic status (SES) (234 cases, 58.5%) followed by middle SES (118 cases, 29.5%) and higher SES (48 cases, 12%). Most of the cases presented with acute infections (234, 58.5%), followed by chronic infections (103, 25.8%) and chronic non-infectious diseases (43, 10.8%). The commonest clinical feature was pallor followed by nonspecific symptoms like generalized weakness and fever, vomiting, abdominal pain, cough. In the pediatric age group, IDA is the commonest type of anemia and is more common in infant and young children especially in lower SES which is similar to other developing countries. In this hospital based study, most cases presented with acute or chronic infections and very few cases presented with complaints related only to anemia. Community based programs might be carried out to increase the awareness of the society about proper nutrition and early detection of anemia.

Keywords: *Pediatric, Microcytic Hypochromic, Iron Deficiency, Anemia*

Cite This Article: Arnab Ghosh, Dilasma Ghartimagar, Sushma Thapa, Brijesh Sathian, and Asis De, "Microcytic Hypochromic Anemia in Pediatric Age Group: A Hospital Based Study in Nepal." *American Journal of Public Health Research*, vol. 3, no. 4A (2015): 57-61. doi: 10.12691/ajphr-3-4A-12.

1. Introduction

There are 2 billion people with anemia in the world and it is estimated that half of all anemia cases are due to iron deficiency. In developing countries, 39% children below 5 years and 48% children between 5 – 14 years suffer from anemia [1]. It is reported that, in Asia, the prevalence of anemia in children below two years of age will possibly surpass 90% of children [2]. In South East Asia, 66% of the children are anemic which results into 324,000 deaths and 12,500,000 Disability Adjusted Life-Years (DALYs) in this area, which makes them the premier in the world [3]. Nepal Ministry of Health and population survey 2011 showed that incidence rates of anemia among children under 5 years and under 6-23 months age to be <40% and 69% respectively [4].

Iron deficiency, other than anemia, also causes impaired cognitive and motor development, behavioral abnormalities and affects school performance. Children with anemia may present in hospital with anemia related nonspecific or specific symptoms or with other associated diseases. Anemia is diagnosed after hemoglobin estimation and further sub typing is done by complete blood counts, peripheral blood smears and other relevant tests as and when required. Iron deficiency anemia (IDA) shows microcytic hypochromic erythrocytes on peripheral smear, which may however also be seen in thalassemia, chronic inflammation, lead poisoning and sideroblastic anemia. In the current study, we have analyzed all pediatric cases with microcytic hypochromic anemia due to iron deficiency.

2. Materials and Methods

This was a hospital based retrospective study conducted in the Department of Pathology during the time period from September 2013 to December 2014. All cases with

age between 1 month to 15 years who were reported as having microcytic hypochromic anemia were included in the study and were evaluated for definite diagnoses. In the current study, criteria for diagnosing anemia was taken as hemoglobin less than 11 g/dl in age less than 6 years and less than 12 g/dl in age 6-15 years [5,6]. Blood samples were received from the pediatric outpatient, ward and emergency. The samples were run with 3 parts coulter machine (manufacturer RFCL India) for complete blood counts. In all cases, peripheral smears were made and stained with Leishman stain. For the definite diagnosis, serum iron studies were carried out in all cases. Bone marrow study and other relevant tests were carried out wherever possible and necessary. All cases with iron deficiency were collated according to age, sex, social status, clinical features and presentation.

2.1. Sample Size Calculation [7]

In a study done prior to the study in 100 patients with reported anemia cases all types showed Expected Proportion of Iron deficiency anemia cases= 65%. 350 patients was required as sample size with absolute Precision (%) = 5, Desired confidence level (%) = 95.

3. Results

A total of 2528 pediatric blood samples were examined during the study period and 632 cases were found to have Anemia. A microcytic hypochromic picture on peripheral smear was seen in 422 cases. After clinical evaluation and laboratory tests, iron deficiency was diagnosed in 400 cases which comprised 63.3 % (400/632) of all Anemia and 94.8% (400/422) of all Microcytic Hypochromic Anemia cases in this age group. Microcytic hypochromic picture was also seen in 5 cases of Thalessemia and 17 hematological malignancies which included 11 Acute Lymphocytic Leukemia (ALL), 3 Hodgkins Lymphoma (HL), 2 Chronic Myeloid Leukemia (CML) and 1 case of Acute Myeloid Leukemia (AML). (Table 1).

Table 1. Hematological Diagnoses of All Cases with Microcytic Hypochromic RBC Picture (N=422)

Diagnosis	n = 422
Iron Deficiency Anemia	400
Thalassemia	5
Acute Lymphocytic Leukemia	11
Hodgkins Lymphoma	3
Chronic Myeloid Leukemia	2
Acute Myeloid Leukemia	1

Among the iron deficiency cases, there were 240 boys and 160 girls with male female ratio of 1.5:1 (Figure 1).

The age range was from 1 month to 15 years with a mean age of 4.9 years. 135 (33.8%) cases were below 1 year of age, 180 (45%) cases were between 1-6 years, which was the commonest age group and 85 (21.2%) cases were above 6 years of age. The majority of the patients were in the lower socio economic status scale (SES) (234 cases, 58.5%) followed by middle SES (118 cases, 29.5%) and higher SES (48 cases, 12%).

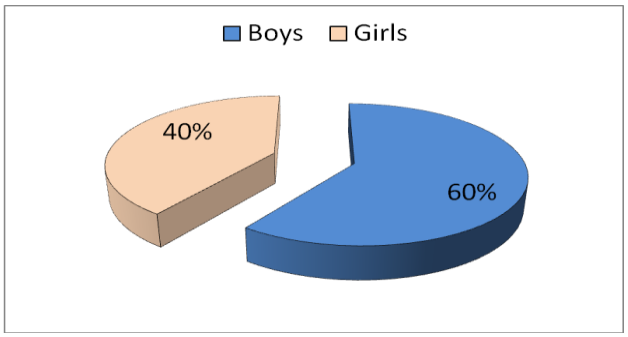

Figure 1. Showing Distribution of Iron Deficiency Anemia in Boys and Girls

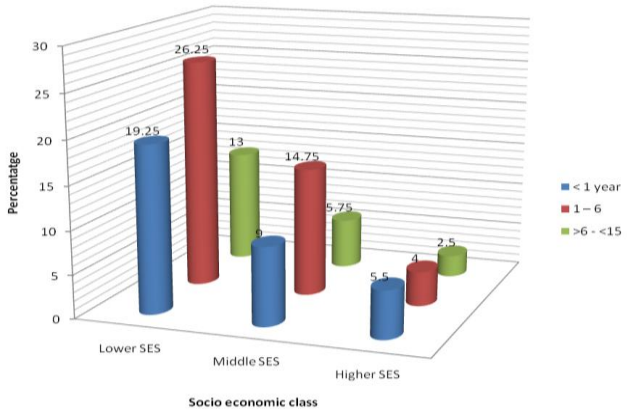

Figure 2. Showing Age Group Distribution of All Iron Deficient Cases (N=400) and Its Correlation with Socio-Economic Status

Table 2 shows the initial clinical presentation in all 400 cases of Iron deficiency anemia. Most cases (234, 58.5%) presented with acute infections including acute upper and lower respiratory infections, acute gastrointestinal infections, acute meningitis, acute urinary tract infections and acute otitis media. Chronic infections were seen in 103 (25.8%) cases which included chronic diarrhea, tuberculosis, recurrent pneumonia and HIV. We had 43 (10.8%) cases who presented with chronic non-infectious diseases including cardiovascular diseases, juvenile rheumatoid arthritis and nephritic syndrome. 8 adolescent girls presented with menstrual irregularities. Thalassemia cases and all malignant cases presented with the main complaint of stunted developmental growth, failure to thrive and organomegaly or lymphadenopathy.

Table 2. Clinical Presentations of All Iron Deficiency Cases (N = 400)

Initial Clinical Presentation	N	%	CI
Acute Infections	234	58.5	(53.67, 63.33)
Chronic Infections	103	25.8	(21.46, 30.04)
Chronic Disease (Non-Infectious)	43	10.8	(7.71, 13.79)
Failure To Thrive	12	3	(1.33 4.67)
Menstrual Disorders	8	2	(0.63, 3.37)
Total	400		

Clinical features of all iron deficient cases have been shown in Table 3. The commonest feature was pallor followed by nonspecific symptoms like generalized weakness and fever, vomiting, abdominal pain, cough.

Table 3. Clinical Features of All Iron Deficient Cases (N=400)

Clinical Features	No of cases	CI
Pallor	346	(83.15, 89.85)
Generalized Weakness	340	(81.50, 88.50)
Fever	247	(56.99, 66.51)
Vomiting	220	(50.12, 59.88)
Abdominal Pain	205	(46.35, 56.15)
Cough	186	(41.61, 51.39)
Protein Energy Malnutrition Features	170	(37.66, 47.34)
Lower Respiratory Tract Infections Features	107	(22.41, 31.09)
Diarrhea (Acute / Chronic)	99	(20.52, 28.98)
Upper Respiratory Tract Infections Features	87	(17.71, 25.79)
Developmental Delay / Weight Loss	83	16.78, 24.72)
Pica	56	(10.60, 17.40)
Glossitis	42	(7.50, 13.50)
Koilonychia/ Nail Features	37	(6.41, 12.09)
Poor Feeding / Failure To Thrive	17	(2.27, 6.23)
Seizure	33	(5.55, 10.95)
Hepatomegaly	8	(0.63, 3.37)
Acute Bleeding /Menstrual Irregularity	7	(0.46, 3.04)
Splenomegaly	6	(0.31, 2.69)
Chronic Bleeding	5	(0.16, 2.34)
Facial Puffiness / Edema	4	(0.02, 1.98)

4. Discussions

Microcytic hypochromic anemia may be due to a defect in heme synthesis or in globin synthesis. In pediatrics, the differential diagnosis is generally limited to one of four diagnoses – iron deficiency, thalassemia, lead poisoning, anemia of inflammation. Sideroblastic anemia also may cause microcytosis but are rarely seen in children. Iron deficiency anemia is by far the most common cause [8].

Iron deficiency anemia is the most common nutritional deficiency in the world. The recent statistics from WHO indicates that up to 80% of the world's population (5 billion) is iron deficient and 30% (2 billion) are anemic as a consequence of iron deficiency. IDA is a public health problem in both developing and industrialized countries affecting about 800 million people in developing countries and 70 million in developed countries [9]. Some published studies report showed that anemia in US and UK is about 2-15%. Recent studies have confirmed high prevalence of IDA in certain groups e.g., in migrant Asian children (up to 29%) even in developed countries.

IDA is more common in South Asian countries including India, Bangladesh and Pakistan than anywhere else in the world. In Asia approximately 70% of world's malnourished children live. Fifty percent of the preschool children are malnourished out of that 64% in Bangladesh and 16% in China. Due to protein energy malnutrition as well as micronutrient deficiency IDA affects 40-50% of preschool children [10]. In Pakistan IDA constitutes 83% of all anemia and is a major nutritional problem. Studies on nutritional status of boys and girls have been conducted in 11 different countries and Anemia prevalence was found to be 55% in India and 42% in Nepal. It is a problem mainly for infants, adolescent girls and women of child bearing ages in developing countries [1,11]. In a study conducted in 2 districts in India, 72% of children aged (12-23 months) had low ferritin level [12,13]. Highest prevalence of anemia was seen in children less than 10 years of age was seen specially in below 5 years of age [13].

More than a third of Nepalese children are born with low birth weight i.e. below 2.5 kg which indicates that their nutritional status is seriously compromised at the time of birth which is primarily a reflection of mothers' poor nutritional status [14]. Despite low birth weight, most children grow well during first 6 months of life due to universal breast feeding practices seen in Nepal. Interestingly. the nutritional status of most children actually further deteriorates after weaning. Breast milk does not fulfill infants' iron needs after 6 months, and supplementary foods tend to be poor in iron content and the iron they contain often has a low bio- availability [4,15]. The risk is increased by prolongation of breast feeding and early introduction of cow's milk. Iron intakes appear to decline between 12-18 months when there is transitional to adult diets and fortified formula is no longer provided [16]. Half of the children in Nepal are found to be chronically malnourished [14]. Similar to India and Pakistan, the most important cause of iron deficiency in Nepal is inadequate intake of iron from diet and the other important causes include chronic infections including diarrhea, chronic bleeding including parasitic infestation such as hook worm [13,14,17,18].

It may also be seen in adolescent girls due to increased menstrual loss. More number of menarcheal girls are found to be anemic than non-menarcheal girls. In a study on adolescent girls, Vasanti et al observed higher prevalence of iron deficiency in menarcheal girls of both urban and rural areas. The pre adolescent boys had a higher prevalence rate as compared to girls of same age. This is perhaps due to the adolescent growth part [19].

Among 400 cases majority (315 cases, 78.8%) were below 6 years of age in the current study. This correlates with other international literature where majority of pediatric anemia was found in infants and young children [20,21,22]. Male preponderance was seen in our study with a male to female ratio of 1.5:1. Muhe L et al had also found male to be affected more in pediatric age group [15]. Iron deficiency anemia generally known to be much more common in lower socioeconomic class. However some studied have concluded high prevalence (40%) of IDA in upper middle and upper class in India as well [17,23]. in our study we found more than half of the patients were in lower SES but 12% of cases were from higher SES. Halileh S et al have concluded in their study that anemia is independently related to low income [24].

The clinical manifestation of anemia is evident when the hemoglobin level falls below 7-8 gm/dl and can be detected on the basis of pallor present on palms, nail beds, conjunctiva, mouth mucosa and tongue [15]. Clinically, pallor correlates well with hemoglobin level. Verma M et al found only 7.5% of anemic children did not show pallor on presentation [17]. In the current study only 55 cases did not show pallor. Non specific symptoms like irritability, palpitation, dizziness, headache and fatigue are quite common in other studies as we have seen in our study as well.

Iron deficiency alters the immune system and make patients more prone to infection. The changes in immune reaction is complex including defective lymphocyte mediated immunity and impaired bacterial killing by phagocytes. Defective cellular immunity is due to reduction in the helper and suppressor T cells [25]. In several studies, it was noted that low hemoglobin especially iron deficiency is an important risk factor of acute infections like lower respiratory tract infections [25,26,27]. Neutrophils also have been noticed to show mark reduction of myeloperoxisdase activity. In our study, majority of the patients presented with complaints of other related disease rather than the features of anemia. In our study, 56.8% cases presented with acute infections and majority of these were respiratory infections. IDA patients are also more prone to chronic or recurrent infections (e.g., chronic diarrhea) which may be due to deficiency of micronutrients. Severe or recurrent infection itself may also lead to iron deficiency [25,28].

Anemia may be associated with fever which can aggravate the negative effects of iron deficiency on the bain and can precipitate seizures [25,29]. We had 247 cases who had fever at the time of reporting and 33 cases had history of or presented with seizures. Pica is characterized by an appetite for substance that are largely non- nutritive. Pica may be of different varieties, as it may be a cultural tradition, acquired taste, or a neurological mechanism such as iron deficiency or a chemical imbalance and helminthic infestations. Crosby et al estimated an incidence of pica in his iron deficient patients in 50% [25]. In our study, we found 56 cases with history of pica. Iron deficiency also impairs growth in children and in one study 50% of iron deficient children had weight below twenty five percentile of expected weight [25]. In our study, we have noticed developmental delay in 80 (20.8%) children. The patients with long standing iron deficiency develop several epithelial lesions affecting nail, tongue, mouth and other parts of GIT and genitourinary parts [16]. In our study we saw 79 (19.8%) cases with nail features and/or glossitis. Vasanti et al in her studied observed higher prevalence of iron deficiency among menarcheal girls. We had only 5 cases of adolescent girls who presented with menstrual disorders [19].

Nepal government has made policies to trim down the factors viz. (1) protein energy malnutrition in children under 5 years of age, (2) the prevalence of anemia among children and adolescent girls, (3) close to get rid of iodine deficiency disorders and vitamin A deficiency and endorse the elimination, (4) the infestation of intestinal worms among children, (5) the prevalence of low birth weight, (6) the grave risk of malnutrition and life during outstandingly complicated conditions. Also to perk up family unit food safety measures to guarantee that all people can have reasonable access, ease of use and using up of food desired for healthy life and health and nutritional grade of school children [30].

5. Conclusion

We have seen that in pediatric age group, IDA is the commonest type of anemia and is more common in infant and young children especially in lower SES which is similar to other developing countries. In this hospital based study, most cases presented with acute or chronic infections and very few cases presented with complaints related only to anemia. Community based studies and programs might be carried out to evaluate the etiological factors and exact prevalence in this age group, as well as to increase the awareness of the society about proper nutrition and early detection of anemia.

Declaration of Conflicting Interests

The authors declare that there is no potential conflicts of interest with respect to the research, authorship and /or publication of this article

Funding

The authors received no financial support for the research, authorship and/or publication of this article

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