Significance of a low mean corpuscular volume in patients in Kuala Lumpur Hospital, Malaysia

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Abstract

A study was carried out to determine the common causes of a low mean corpuscular volume in patients admitted to Kuala Lumpur Hospital between 1 January and 30 June 1998. A total of 2097 microcytic cases were selected based on a mean corpuscular volume of less than 76 fL as determined by the Abbott CELL-DYN ® 1700 System Electronic Cell Counter. Iron deficiency (50%) is the most common cause of microcytic anaemia, followed by chronic diseases (21%), and thalassaemia syndromes (20%). Iron deficiency anaemia is still relatively prevalent (16.3%).

Key words: microcytic anaemia; iron deficiency anaemia; corpuscular volume

Introduction

Microcytosis is a classical feature of iron deficiency anaemia and thalassaemia syndromes. It is a laboratory finding frequently encountered in approximately 3% of admissions ro metropolitan general hospitals (Cunningham & Rising, 1977).

Iron deficiency anaemia, a major nutritional and significant world-wide public health problem particularly in developing countries is the most common cause of microcytic anaemia (Yip, 1994). Iron deficiency was estimated ro involve half of women and children, and up to a quarter of men in developing countries (De Maeyer, 1989). In the Unired States, iron deficiency anaemia is relatively common in toddlers, adolescent girls, and women of reproductive age especially in those who are minority, low income, less educated, and multiparous (Looker *et al.*, 1997).

Thalassaemia and haemoglobinoparhies are common in South East Asia. In Thailand the frequency of β-thalassaemia is 3-9% (Torcharus *et al.*, 1993). Haemoglobin E reaches a frequency of 75% in Northeast Thailand (Thein, 1997). In Peninsular Malaysia β-thalassaemia trait was found in 2.18%, Hb E 3.49% and α thal$_2$ (α+) trait in 26% of Malays (George & Khuziah, 1984). A common thalassaemic haemoglobinopathy is Haemoglobin Constant Spring which is due ro a single base substirution in α_2 globin termination codon (Thein, 1997).

In the present study, the common causes of a low mean corpuscular volume in patients admitted to Kuala Lumpur Hospital were determined based on full blood cell count results and specific laboratory tests. The second targer was to assess the prevalence of iron deficiency anaemia in Kuala Lumpur Hospital. The hypothesis is that an improved living standard is associated with less cases of iron deficiency anaemia in the urban setting of Kuala Lumpur.

Materials and Methods

Subjects

Retrospective and prospective reviews of patients' records were obtained between 1 January and 30 June 1998 in the Haematology Laboratory of the Blood Service Centre, Kuala Lumpur Hospital. Patients (n = 2427) with a mean corpuscular volume (MCV) equal to or less than 76fL, as determined by Abbott CELL-DYN ® 1700 System were initially selected. A preliminary screening was conducted and 330 (13.6%) from the total cases were excluded as complete records of patienr's particulars could not be traced. Subsequent patient's visits were not included in the analysis. The final total microcytic cases observed within the six months were 2097.

Variables

Venous blood samples obtained on the first attendance were collected into EDTA (K_3) vacutainers. Fresh whole blood specimens were studied with the use of the Abbott CELL-DYN ® 1700 System electronic counter, which measured and reported the red blood cell indices in a printed format. The diagnosis of iron deficiency anaemia was based on a serum ferritin level of less than 10 ng/mL as determined by the Abbott IMx® Ferritin Assay System. Thalassaemia syndromes were confirmed through 'H' inclusion test, cellulose acetate haemoglobin electrophoresis at pH 8.4, and further quantification of haemoglobin A_2 and F concentrations.

Statistical Analyses

Data was evaluated using SPSS version 8.0 to compare the frequency among the erhnic groups, age-sex groups, and aetiology among the cases of microcyrosis.

Results

Common causes of microcytosis

Over the six months, the number of patients studied was 6426. Of the 6426 patients, 2097 (32.6%) were microcytic cases, 1049 (16.3%) iron deficiency anaemia (IDA), 447 (7.0%) anaemia of chronic diseases (ACD), 427 (6.6%) thalassaemia syndromes and haemoglobinopathies, and 174 (2.7%) with undetectable cause (Table 1).

The majority of iron deficient patients were in Malays (7.9%) and Indians (6.1%). Among the age-sex groups, the greatest number of iron deficiency anaemia cases occurred in 54.6% women (567/1039), followed by 16.2% men (168/1039)), 12.0% children (126/1039), 7.3% girls (76/1039), 6.7% infants (70/1039), and 3.1% boys (32/1039) (Table 2).

In the thalassaemia syndromes and haemoglobinopathies, β thalassaemia trait was the most prevalent (44.3%), which occurred highest among the Malays (26.9%) (Table 3). Beta thalassaemia trait accompanied by increases in haemoglobin A_2 with a mean percentage of 5.43 ± 0.83 was detected in 169 (39.6%) of the patients, while increases in haemoglobin F with a mean percentage of 5.42 ± 3.35 were detected in 26 (6.1%) of the patients.

Haemoglobin E trait (22.2%) were seen mostly in the Malays (19.2%) and Aborigines (1.9%). Haemoglobin Constant Spring trait (1.6%), Haemoglobin D - β thalassaemia trait (0.2%), and Homozygous Haemoglobin E (0.7%) occurred only among the Malays (Table 3).

The only one case of Haemoglobin D – β thalassaemia trait showed an increase in the mean percentage haemoglobin A2 (4.6%). The 5 cases (1.2%) of β intermedia have a normal haemoglobin A_2 but an increase in haemoglobin F, with a mean percentage of 27.84 ± 22.61.

The number of patients with α_1 thalassaemia trait accounted for 76 cases (17.8%), all of which showed occasional 'H' inclusions and were mainly observed in the Chinese (11.7%) and Malays (5.6%). In addition, numerous 'H' inclusions were detected in 14 cases (3.3%) of Haemoglobin H disease, and 6 cases (1.4%) of Haemoglobin H – Haemoglobin Constant Spring trait (Table 3).

In the anaemia of chronic diseases, the highest number was among the Malays (61.1%), followed by the Indians (18.6%), Chinese (15.4%), and the Aborigines (0.7%) (Table1).

Prevalence of iron deficiency anaemia

The trend of iron deficiency anaemia in Kuala Lumpur Hospital has decreased since the beginning of 1980s and fluctuated between 10 to 12%. However, at the turn of the decade, the percentage increased to approximately 18%. As compared to the mid-year of 1998, iron deficiency anaemia cases remained at a slightly lower level of 16.32% (Table 4).

Table 1. Common causes of microcytosis among ethnic groups

Causes	Malay	Chinese	Indian	Aborigine	Others	Total/Cause
IDA	510	103	393	12	31	1049
ACD	273	69	83	3	19	447
Thalassaemia	260	137	14	13	3	427
Unclassified	121	24	21	3	5	174
Total/Group	1164	333	511	31	58	2097

Table 2. Distribution of gge-sex groups in iron deficiency anaemia*

Group (years)	Malay	Chinese	Indian	Aborigine	Others	Total
Infants, 0-1	55	3	9	2	1	70
Children, 1-9	75	11	32	3	5	126
Boys, 10-19	17	1	13	-	1	32
Girls, 10-19	35	2	36	2	1	76
Men > 20 168	81	39	40	2	6	168
Women > 20	242	46	258	4	-	567

* Ten cases were excluded as age was not available.

Table 3. Distribution of thalassaemia syndromes and haemoglobinopathies by ethnic groups

Diagnosis	Malay	Chinese	Indian	Aborigine	Others	Total
α_1 trait	24	50	1	1	-	76
Hb CoSp trait	7	-	-	-	-	7
Hb H - Hb CoSp	-	4	2	-	-	6
Hb H disease	5	9	-	-	-	14
β trait	115	61	10	2	1	189
β intermedia	2	2	-	-	-	4
β major	7	5	-	2	1	15
Hb D - β trait	1	-	-	-	-	1
Hb E trait	82	3	1	8	1	95
Homozygous Hb E	3	-	-	-	-	3
Unclassified	14	3	-	-	-	19

Table 4. The percentage of iron deficiency anaemia cases in Kuala Lumpur Hospital from 1980 to 1990, and Mid-year of 1998.

Year	Total Annual Cases	Total IDA Cases	Percentage of Annual IDA Cases (%)
1980	9357	1861	19.89
1981	10700	2116	19.78
1982	12205	1417	11.61
1983	9981	1077	10.79
1984	9838	1148	11.67
1985	10886	1197	11.00
1986	12769	1306	10.23
1987	11599	1193	10.29
1988	12137	1218	10.04
1989	11824	1372	11.60
1990	13544	2447	18.07
1998	6426	1049	16.32

Discussion

Studies have shown a substantial reduction over the last 20 years in the prevalence of iron deficiency anaemia among infants and young children from economically constrained families (Yip *et al.*, 1987). In Malaysia, this problem has been identified in high-risk groups comprising of children, pregnant mothers, the underprivileged, and those with hookworm infestation (Chong *et al.*, 1984).

Prevalence figures published by WHO (1992) showed that a high proportion of women of childbearing age suffer from iron deficiency anaemia, where menstrual blood loss and the increased iron requirements of pregnancy are the major factors.

Infants and preterm new-borns represent major risk groups due to their low iron stores at birth, high iron requirements for growth, and diets consisting of foods with low iron content and bioavailability (Dallman *et al.*, 1980). Furthermore, documented evidence of early weaning and replacement with pasteurised milk inducing microscopic faecal blood loss (American Academy of Paediatrics, Committee on Nutrition, 1992) and the cow milk protein and calcium content as potent inhibitors of iron absorption (Montalto *et al.*, 1985) may contribute to iron deficiency anaemia in infants.

The prevalence of iron deficiency anaemia in adult men and postmenopausal women is usually the result of chronic blood loss from gastrointestinal tract (Van der

Weyden *et al.*, 1990). In addition, the frail elderly are vulnerable due to increased blood loss, poor eating habits, and impaired iron absorption (Looker *et al.*, 1997), whereas young children are at risk because of rapid growth and insufficient iron in diet.

Genetic disorders of haemoglobin synthesis are not uncommon in Malaysia. The frequency of α_1-gene mutation in the main ethnic groups of Peninsular Malaysia have been long established with the highest percentage occurring among the Chinese (5.1%), followed by the Malays (3.2%) and Indians (1.1%) (Lie-Injo and Ti, 1961).

An abnormal β-chain variant commonly found in Malaysia is Haemoglobin E. The gene frequency exists highest among the Malays (2 to 15%) and Aborigines (8 to 54%) (Lie-Injo, 1969). In addition, coexisting Haemoglobin H disease with Haemoglobin Constant Spring was elucidated to prevail among the Malays (2.2%) and Aborigines (6.2 to 6.6%) (Lie-Injo *et al.*, 1974), which is contraty to the result as it was observed only in the Chinese and Indians (4 cases and 2 cases respectively).

Thalassaemia is recognized as a growing problem in the majority of countries in the Sourheast Asian region. The approach in addressing this was to focus worldwide efforts on preventive measures such as healthy carrier screening and genetic counseling primarily found in antenatal clinics, and the prenatal diagnosis with induced termination of affected pregnancies (Embury, 1995). It is essential that the disorder be recognized early for appropriate provision of maternal health care and preventive measures to communities.

Controlling iron deficiency requires the coordination of nutrition and primary health care programmes as part of an integrated approach to improve health and nutrition of the population. From the individual, public health, and policy perspectives, accurate assessment of iron status is important for the prevention and control of iron deficiency anaemia, and for planning and evaluation of intervention programmes.

Although well-established biochemical tests for assessing iron status are present, the cost and interference from infectious conditions make it difficult in many developing country settings (Yip, 1994) making the understanding of the aetiology even more complex. The examination of bone marrow aspirates for iron content is considered the gold standard for assessing iron status (Hillman & Finch, 1985) which however, involves invasive and expensive technique in clinical investigations, and is impractical for use in field studies.

In summary, iron deficiency anaemia is predominantly observed among the Malays (24%) and Indians (19%), and in women of reproductive age (54.6%). The anaemia of chronic diseases is mainly seen in Malays (61.1%). Among the thalassaemia syndromes, the highest number of patients are observed in the Malays with β thalassaemia trait (5%), followed by the Malays with Haemoglobin E trait (4%) and the Chinese with α thalassaemia trait (2%).

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