A hematological survey of preschool children of the United Arab Emirates

Campbell J. Miller, FRACGP, MSc Comm Med. Earl V. Dunn, CM, FCFP(C).
Bertel Berg, MD. Sameeh F. Abdouni, Dip Med Lab.

ABSTRACT

Objective: Anemia is common worldwide, particularly in developing countries including states of the Arabian Peninsular. The purpose of this study was to produce a hematological profile of preschool national children of the United Arab Emirates (UAE).

Methods: From April 2000 to October 2000, a cross-sectional community clinic-based capillary blood survey was carried out on a convenience sample of 1-5-year-old Emirati children attending a Primary Health Care Center in Al-Ain, UAE. Those children with capillary hemoglobin (Hb) and mean corpuscular volume (MCV) values below predetermined cutoffs were offered venous blood hematological workup. A random sample of children with values above those cutoffs were also offered the same workup. All venous blood sampling was completed by May 2001.

Results: Four hundred and ninety six children were surveyed. The mean Hb and adjusted MCV rose with increasing age but were not significantly different by gender. Two hundred and sixty-two children with Hb or MCV below the cutoffs and 50 children above the cutoffs were venous blood tested. The estimated abnormalities for this population of children were as follows: anemia 36.1%; iron deficiency anemia 9.9%; glucose-6-phosphate dehydrogenase (G6PD) deficiency 9.1%; sickle cell trait 4.6%; and beta thalassemia 8.7%. There was likely to be a high prevalence of alpha thalassemia.

Conclusion: Rates of anemia and iron deficiency anemia in this population of children were consistent with other reports from the region, but higher than in developed countries. Hereditary red cell abnormalities were common, particularly G6PD deficiency. The gene frequency of alpha thalassemia is likely to be high but requires DNA studies.


Anemia in childhood is an important problem worldwide. There is evidence that iron depletion with or without anemia has detrimental effects on the normal growth and psychomotor development of children. The United States National Health and Nutrition Examination Survey revealed a 9% prevalence of iron deficiency and 3% prevalence of iron deficiency anemia in one to 2-year-old children. Anemia and iron deficiency states in children are common in developing communities including expatriates of such communities residing within developed nations. Studies of Middle Eastern populations have shown high prevalence of anemia and iron deficiency in preschool children. Padmanabhan et al recently reported an anemia prevalence of 45.1% in a hospital outpatient-based study of 153 apparently healthy 3-5-year-old Omani children. Very few of these children had evidence of iron deficiency and the authors considered that alpha thalassemia was a major contributor to the anemia. Reports of similar studies in the United Arab Emirates (UAE) are few: Hossain et al reported anemia (hemoglobin [Hb] <11.0g/dl) in 35% of 193 multiracial children aged 6-22 months in the UAE city of Al-Ain. A large study of 11,802 6-year-old children from 6 of 7

From the Department of Family Medicine (Miller, Dunn), Department of Pathology (Berg), Faculty of Medicine and Health Sciences, United Arab Emirates University, and the Department of Primary Health Care (Abdouni), Ministry of Health, Al-Ain, United Arab Emirates.

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Address correspondence and reprint request to: Dr. Campbell J. Miller, Department of Family Medicine, Faculty of Medicine and Health Sciences, United Arab Emirates University, PO Box 17666, Al-Ain, United Arab Emirates. Tel. +971 (3) 7039585. Fax. +971 (3) 7671890. E-mail: cjmiller@uaeu.ac.ae

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Emirates of the UAE showed that 33% of the Emirati children had Hb levels of <12.0g/dl. Genetic abnormalities of the red cell may present as serious clinical problems including anemia, and in countries where consanguinity is prevalent, they represent important population health issues. Clinical experience and existing reported data indicates that both consanguinity and genetic abnormalities of red cells are common in Arabic populations of the Middle East, particularly in UAE. For the purposes of this study, we have defined anemia according to World Health Organization (WHO) and UNICEF criteria, as a Hb <11.0g/dl for children 12-59 months, <11.5g/dl for children 60-71 months. Microcytosis was defined by age group as follows: mean cell volume (MCV) <70fl for infants <24 months, <73fl for children 24-59 months, and <75fl for children ≥60 months. Iron depletion was defined as a plasma ferritin <10µg/l, iron deficiency as iron depletion plus an erythrocyte zinc protoporphyrin (ZPP) of >40 µmol/mol heme. Iron deficiency anaemia was defined as iron deficiency plus anaemia. The aim of this study was to produce a hematological profile of Emirati children aged 1-5 years who attended a primary health care centre (PHCC) in Al-Ain, UAE.

**Methods.** A cross-sectional community clinic-based capillary blood sample survey was carried out over a 6-month period from April 2000 to October 2000. Based on predetermined capillary Hb and MCV cutoff levels, parents of those children falling below those cutoffs were invited to submit their children for venous blood hematological workup. In addition, the parents of a random sample of children whose capillary Hb and MCV were above the cutoffs were invited to submit their children for venous blood testing. All capillaries and venous blood sampling were completed by May 2001.

**Study population.** A convenience sample of Emirati children aged 12-71 months was surveyed. The children were born of parents who identified themselves as Emirati and who held UAE passports. The parents and children were attending one urban PHCC in Al-Ain, UAE. All children attending for any reason, including for vaccination or simply accompanying another family member, were included. There were no exclusions but parents were required to have a current health card to facilitate blood testing.

**Sample size.** Using a predicted anemia prevalence of 24%, a sample of 450 would have provided an anemia estimate of 20-28% with 95% confidence. For the children with "normal" initial Hb and MCV, we based our sample size on an estimated 7.5% prevalence of glucose-6-phosphate dehydrogenase (G6PD). A sample of 50 would have given us an estimate of 3-11% with 80% confidence.

**Hematological testing.** Finger prick capillary blood samples were collected in the PHCC by any one of 5 laboratory technicians. The samples were tested for Hb and MCV using a Coulter Counter CBC-5. The accuracy of the cell counter was tested against the Al-Ain Hospital Coulter counter STKS using 10 patient blood samples. Intraday precision was estimated running 20 tests on each of 3 blood samples with low, mid-range, and high Hb and MCV results. Capillary Hb and MCV results by Coulter CBC-5 counter were compared with venous blood Hb and MCV results from the same patients by Coulter STKS using paired samples of venous and capillary bloods drawn from clinic patients. For the purposes of offering a follow up hematological workup using venous blood, it was decided to set the adjusted cutoffs for Hb at 11g/dl for children aged 12-59 months, 11.5g/dl for children aged ≥60 months, and an MCV of 80fl. These values were used to identify groups of "normal" and "abnormal" children. All venous blood samples were collected by one technician using 23 gauge scalp vein infusion sets. Samples were transferred to ethylenediaminetetraacetic acid (EDTA) tubes and transported to the hospital for the following analyses: complete blood count including red cell distribution width (RDW), reticulocyte count, erythrocyte ZPP, high performance liquid chromatography (HPLC) analysis for hemoglobinopathies, and G6PD screening test. In addition, 0.5-1 ml of blood was transferred to a plain tube, centrifuged and the serum frozen at -5°C for later ferritin assay. Complete blood counts were analyzed in a Coulter Counter STKS (Coulter), reticulocytes in a Coulter Counter Gensys (Coulter), ZPP in a front surface AVIV hematofluorometer, ferritin by an automated enzyme linked fluorescent assay (Vidas Ferritin, bioMerieux Vitek, Missouri, USA), hemoglobin HPLC in Biorad Variant, G6PD screening test by fluorescence.

**Data analysis.** Results were analyzed using SPSS for Windows version 11 software. Student’s t-tests and analysis of variance (ANOVA) were used for differences in means between groups. Pearson’s correlation coefficients (r) were used to determine relationships between continuous variables. The study was approved by the Research Ethics Committee of the Faculty of Medicine and Health Sciences, UAE University. Parents of the children gave written informed consent. All blood test results were sent to the clinic for patient follow up.

**Results.** There was high correlation between the clinic and hospital Coulter counters for Hb (r=0.90) and MCV (r=0.98). Accuracy of the Coulter CBC-5 was within 9.5% and 6.5% for Hb and MCV for all 10 blood samples. The tests of precision revealed coefficients of variation of ≤2% for Hb and ≤3.9% for MCV across low, mid-range, and high value blood samples. Comparisons between the clinic capillary and hospital venous results showed the mean Hb for both counters in the 10 samples were within 0.1g/dl. Mean MCV results were 3.7fl lower in the clinic counter than for the venous blood measured by the hospital counter. Therefore, all clinic Hb values were reported as measured. Mean cell volume values are reported adjusted by +4fl. Four hundred and ninety six children were screened by
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Discussion. The estimated anemia prevalence of 36.1% in this study was consistent with 2 previous studies carried out on slightly different age groups of children in the UAE.\textsuperscript{15,16} A recent Omani study\textsuperscript{23} and a Saudi study performed more than a decade ago.\textsuperscript{12} This prevalence is midway between the rates (≤3%) reported in the United States of America\textsuperscript{4} and Australia\textsuperscript{24} and the high prevalence of some developing countries, for example 72.5% for 1-4 year old children reported from Uzbekistan in 1998.\textsuperscript{9} In countries with high prevalences of hemoglobinopathies, such as UAE, HB measurement is not a valid indicator of iron status. Padmanabhan et al\textsuperscript{14} reported that out of 153 Omani preschool children, 45.1% were anemic but <2% were iron depleted by our definition. They concluded that alpha thalassemia was a major contributor to the prevalence of anemia in their study population. The discrepancy, in our study, between estimates for anemia, iron deficiency anemia, and microcytosis of 36.1%, 9.9%, and 53.8%, would suggest a wider differential diagnosis of anemia than iron deficiency in our population. Another possibility is that the international criteria for anemia, iron deficiency, and microcytosis do not apply in UAE. There are considerable discrepancies in the literature regarding reference values for HB, MCV, serum ferritin and erythrocyte ZPP and no published data on such values exist for Middle Eastern populations of children. In particular, ZPP cutoffs for normality range from 40-80 µmol/mol of heme.\textsuperscript{22,24} Recalculating our estimates of iron deficiency and iron deficiency anemia using the appropriate age group, microcytosis and low MCH instead of ZPP values enabled a comparison with the Karr et al\textsuperscript{11} study of 12-38-month-old Australian children of Arabic background. Their prevalence of iron depletion was 23%, iron deficiency were 9% and iron

capillary blood testing, comprising 264 males (53.2%) and 232 females (46.8%). Table 1 outlines the mean HB and adjusted MCV results by age. Mean HB and MCV values rose with increasing age (ANOVA tests of linearity p<0.001) but were not significantly different by gender. Of the 496 children screened, 284 (57.3%) were found to have HB or MCV levels which fell below the cutoff points. Of these, 262 (92.3%) had venous blood samples taken for hematological workup. For those with "normal" HB and MCV results, 50 of the first 94 parents agreed to the venous blood testing of their children. There were no significant differences between venous blood tested and untested "normals" for mean age, birth weight, capillary HB and MCV. Males were more represented in the tested versus the untested group (62% versus 52.5%). Using capillary blood screening in the primary health care clinic, 173 (34.9%) of our sample of children were "anemic" according to WHO/UNICEF standards. Ninety-four (35.6%) boys were "anemic" compared with 79 (34.1%) girls. Two hundred and eighty (56.5%) children had an adjusted capillary MCV <80fl. One hundred and fifty-six (31.5%) had microcytosis as defined above and 41 (8.3%) had microcytosis without anemia. Of the 284 children with capillary HB or MCV which fell below our cutoffs, 262 (92.3%) were venous blood tested. The following abnormalities were demonstrated: 137 (52.3%) were anemic, and 196 (74.8%) were microcytic. Of the 261 tested, 22 (8.4%) had G6PD deficiency, of whom 9 were females. Nine (3.5%) of the 259 tested had sickle cell trait. Excluding those with sickle cell trait, 26 (10.4%) of 225 had HbA2 >3.5% indicative of beta thalassemia trait, and 1 had HbD trait. Six (12%) children had serum ferritins <10µg/l, 2 (4%) were iron deficient, and one (2%) had iron deficiency anemia. Thirty-nine of 297 children tested had a reticulocytosis >2% possibly indicating mild hemolysis. Twenty of these were anemic and 8 had G6PD deficiency. The cause of the 2 highest reticulocyte counts (both 6.6%) was unknown (G-6-PD deficiency and hereditary spherocytosis were excluded). By extrapolating the figures in the 2 tested groups of children to the whole sample of 496 children, it was possible to estimate the prevalence of abnormalities in this population as determined by venous blood testing: anemia 36.1%, microcytosis 53.8%, G6PD deficiency 9.1%, sickle cell trait 4.6%, beta thalassemia 8.7%, iron depletion 26%, iron deficiency 12.7%, and iron deficiency anemia 9.9%.

Table 1 - Mean hemoglobin and adjusted MCV by age group.

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>n</th>
<th>Mean HB (g/dl) (SD)</th>
<th>Mean adjusted MCV (fl) (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-23</td>
<td>126</td>
<td>10.9 (1.3)</td>
<td>72.6 (7.9)</td>
</tr>
<tr>
<td>24-35</td>
<td>121</td>
<td>11.1 (1.2)</td>
<td>74.5 (8.0)</td>
</tr>
<tr>
<td>36-47</td>
<td>107</td>
<td>11.7 (1.1)</td>
<td>76.3 (6.7)</td>
</tr>
<tr>
<td>48-59</td>
<td>102</td>
<td>11.7 (1.2)</td>
<td>77.2 (9.6)</td>
</tr>
<tr>
<td>60-71</td>
<td>40</td>
<td>11.9 (1.1)</td>
<td>76.9 (8.8)</td>
</tr>
<tr>
<td>Total</td>
<td>496</td>
<td>11.4 (1.2)</td>
<td>75.2 (8.3)</td>
</tr>
</tbody>
</table>

MCV - mean corpuscular volume, HB - hemoglobin
deficiency anemia were 6%. The UAE study estimates for the same parameters were 31.3%, 16.5%, and 15.5%, suggesting that the iron status of our population of children was worse than that of Sydney children of Arabic descent. The estimates of anemia, microcytosis, iron depletion and iron deficiency in this study must be interpreted with caution. For logistic reasons, venous blood testing was frequently delayed after the capillary blood screening was carried out. In many cases, this was a matter of weeks, but for those children with "normal" capillary Hb and MCV values, the delay was frequently a matter of months until an adequate sample size was obtained. Under these circumstances, the relationship between the capillary and venous blood results was less certain and could partly explain discrepancies between clinic and hospital Hb and MCV results for the same individuals. Serum ferritin levels are transiently elevated in the presence of inflammatory/infectious diseases. As children with infections were not excluded from our study, some ferritin results may have been spuriously high. This may have resulted in an underestimate of the prevalence of iron depletion, deficiency and iron deficiency anemia in the study. Recently reported community-based studies of the prevalence of G6PD deficiency, sickle cell and thalassemia disorders in some Peninsular Arab states are few. For G6PD deficiency, prevalences have variously been reported as 2-65%, for Saudi, 5-33%, for Oman, 6% for Yemen and 8% for UAE. Our prevalence estimate of 9.1% is consistent with the latter UAE figure, however an Abu Dhabi, UAE hospital-based study of consecutive patients in the late 1970s revealed a G6PD deficiency frequency of 25%. Seven percent of the cases were female. Thirty-seven percent of our cases were female. Given that it is an x-linked genetic abnormality, presumably this frequency in females was an expression of the high levels of consanguinity in the UAE population. The 27 children with G6PD deficiency had only a slightly higher mean reticulocyte count and slightly lower mean hemoglobin level than those without the enzyme defect. Although G6PD deficiency was common in this population, these results go against the common clinical belief that it is a common cause of anemia. Prevalences of the sickle cell gene have been reported as <1-25%, for Saudi, 4-6% for Oman, 1% for Yemen and 2% for UAE. Our study estimate of 4.6% was certainly of the same order as the previous report. Our estimate of 7.9% for the prevalence of the beta thalassemia gene was consistent with that reported in Kingdom of Saudi Arabia (1-13%) and rather greater than the Omani and Yemeni equivalents (1.5% and 1%). Given that levels of HbA2 tend to be lower in the presence of iron deficiency anemia, we were likely to have underestimated the prevalence of beta thalassemia trait in this population of children. Given the necessity for DNA analysis, estimating the gene frequency of alpha thalassemia is more problematic. El-Hazmi and Warsy quote estimated frequencies of up to 55% for Saudi, 67% for Oman, 14% for Yemen, and 28% for UAE. These estimates were usually inferential and based on assumptions on what were thought to be normal ferritin, MCH and MCV values. El Kalla and Baysal reported a gene frequency for alpha thalassemia of 49% in a neonatal screening survey involving 418 consecutive cord bloods from UAE nationals. In our venous blood data, if all children with iron depletion (namely serum ferritin <10µg/l) and indices suggestive or diagnostic of beta thalassemia, sickle cell trait and G6PD deficiency were excluded, 56.3% of the remaining 151 children had MCV values defined as microcytic. This suggested that alpha thalassemia was likely to be of high prevalence in this population of Emirati children.

In conclusion, it cannot be claimed our study population was representative of UAE preschool children. However, it was an hematological survey involving a sizeable community clinic-based sample of Emirati children in an age group infrequently reported on in the literature. Rates of apparent anemia and iron deficiency in our population of one to 5-year-old children were consistent with other regional studies of young children, and were higher than in developed countries. Hemoglobin levels rose with increasing age but were not related to gender. Hereditary disorders of the red cell were common, particularly G6PD deficiency. Deoxyribonucleic acid studies are required to determine the suspected high gene frequency of alpha thalassemia.

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