Anemic or not?

Tiraje Celkan[1], Emel Gür[2], Günay Can[3], İnci Yıldız[1]

Departments of [1]Pediatric Hematology-Oncology, [2]Social Pediatrics and [3]Biostatistics, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

SUMMARY: Celkan T, Gür E, Can G, Yıldız I. Anemic or not? Turk J Pediatr 2003; 45: 329-334.

Laboratory data obtained from blood analysis by an electronic cell counter is a routine test along with physical evaluation. We assessed the hematological characteristics of schoolchildren to establish the prevalence of anemia in İstanbul. The study was performed on 1,600 students between the ages of 6-16. Hematological parameters of all the students were measured by an electronic cell counter on blood taken intravenously. Anemia prevalence was primarily determined according to Dallman's criteria. The results showed that if hemoglobin (Hb) was used as the primary criterion to define anemia, 423 students (27.6%) were found anemic; if hematocrit (Hct) was used, 625 students (40.8%) were found anemic and if mean corpuscular volume (MCV) was taken as a criterion to define microcytosis, 121 students (7.9%) remained below the normal level. The difference of anemia prevalence was high ($p<0.001$) when two evaluation criteria (Hb or Hct) were compared. Furthermore it is known that a 3% difference occurs when automated and spun Hct values are compared. When a correction was made by adding this 3% to our series' Hct values, the anemic students' number decreased to 418 and the ratio became 27.3%, quite similar to Hb criterion ratio. Population based screening surveys for anemia must be designed and compared cautiously taking into account the method used (electronic counters or gravity based centrifuges), otherwise misleading results can be achieved. We evaluated the data of the survey according to different cut-off values and tried to select the proper one for our conditions.

Key words: anemia, cut-off margins, electronic cell counters.

The most widespread nutrition problem in the world is anemia[1,2]. At least one billion people have been estimated to be anemic (10-20% of the world population). Pregnant women and preschool children with anemia reach a ratio of 50-60% in developing countries[2-10]. Although recent studies have indicated a decline in developed countries, the worldwide prevalence of anemia has not changed[5,6].

The screening method and criteria for identifying and defining anemia is different in surveys from different centers[7-14].

Nowadays, widespread use of electronic cell counters makes various hematological values routine parameters. The interpretation of these values needs more accurate cut-off degrees. In order to use routine erythrocyte measurements (Hb, Hct, RBC, MCV, MCH, MCHC) effectively and prevent unnecessary further investigations, misleading or borderline values, interpretation criteria become very important. The type of blood taking (venous or capillary) and the technique used may lead to a possibility of error during interpretation[15].

In this study, we investigated the prevalence of anemia among 6-16-year-old children living in different areas of İstanbul. We evaluated and compared the results according to different cut-off values for anemia.

Material and Methods

The present cross-sectional study on primary schoolchildren living in İstanbul was performed between January 1999 and September 1999 at

Cerrahpaşa Medical Faculty, Pediatrics Department, in collaboration with the Ayhan Şahenk Foundation.

There are 1,431,797 primary school students in İstanbul. Taking the lowest anemia prevalence in our country as 5% and sampling error as 1% at 95% confidence interval, the lowest number of students that is representative of the total is found to be 1,471.

As İstanbul covers a large area, cluster sampling was performed according to the geographical location of the city's central districts. Thus, seven out of 28 central districts in İstanbul were selected. In these seven districts 14 primary schools were chosen by systematic sampling and in each school, classrooms were randomly selected according to age groups. The study was composed of 1,600 primary schoolchildren aged between 6-16 years. Venous blood samples were transported in EDTA containing tubes to Cerrahpaşa Medical Faculty, Pediatrics Department, Hematology Laboratory under suitable conditions, and the blood was analyzed by an automated cell counter for complete blood cell count (Coulter MD 2). Anemia prevalence was determined according to classical Dallman criteria[17] (Table I) and another more simplified Dallman criteria (for this paper these cut-off values will be mentioned as simplified criteria of Dallman) (Table II)[18]. Anemia was also determined according to Who anemia criterion cut-off values [Hb<110 g/L, Hct<33%-an old-fashioned cut-off value which is currently used for women, infants and children (WIC) younger than five years]; Hb<120 g/L, Hct <38%; and 3,16 Hct <36% and MCV<75 fL.

Table I. Classical Dallman Criteria for Anemia[17]

	Hb (g/dl)		Hct (%)		MCV (fL)	
Age	Mean	–2SD	Mean	–2SD	Mean	–2SD
0.5-2	12.5	11	37	33	77	70
2-5	12.5	11	38	34	79	73
5-9	13	11.5	39	35	81	75
9-12	13.5	12	40	36	83	76
12-14						
Female	13.5	12	41	36	85	78
Male	14	12.5	43	37	84	77
14-18						
Female	14	12	41	36	87	79
Male	15	13	46	38	86	78

Table II. Simplified Dallman Criteria for Anemia[18]

Age	Hct (%)	MCV (fl)
6-11	<35%	<77
12-16 female	<36%	<78
12-16 male	<37%	<78

Statistical Analysis: Chi-square, Student's t test and ANOVA were used for analysis. Dallman criteria were taken as the basic parameters for each evaluation cut-off borders while sensitivity, specificity; positive and negative predictive values; and accuracies were calculated.

Results

Blood samples were collected from each student. Sixty-nine samples were not taken into account because of technique; the remaining samples from 1,531 children were considered for the study. The distribution of children and mean Hb, Hct and MCV values according to age and sex are presented in Table III (a, b, c). An increase

Table IIIa. Mean Values According to Age and Sex for the Whole Group and for 6-9 Years

			6-9 years				
	Boys	Girls	Mean	Boys	Girls		
N	798	733	514	268	246	t	p
Mean Hb	12.42±0.96	12.22±1.00	11.90±0.87	11.91±0.83	11.88±0.9	0.447	0.655
(range)	(7.70-17.10)	(5.90-15.40)	(8.20-14.50)	(9.1-14.1)	(8.2-14.5)		
Mean Hct %	36.40±2.69	35.91±2.73	34.95±2.46	35.01±2.33	34.87±2.59	0.633	0.527
(range)	(24.70-47.80)	(20.90-48.50)	(24.10-41.40)	(26.2-41.4)	(24.1-41.3)		
Mean MCV fL	80.86±4.05	81.09±5.32	79.72±4.40	79.67±4.04	79.77±4.76	–0.237	0.813
(range)	(56.60-94.30)	(51.80-97.0)	(51.80-91.20)	(56.8-88.2)	(51.8-91.2)		

in the average Hct and Hb and a decrease in the prevalence of low Hct occurred with increasing age (Table III a, b, c). As expected, the Hb and Hct values of boys were found higher than girls for 12.5-16 years ($t=3.775$ and $t=3.29$ respectively; $p<0.001$) and for 9.5-12 years there was a significant difference for Hb only ($t=2.49$; $p<0.013$) (Tables III b, III c). Although mean MCV of boys was lower than girls (80.86 fL to 81.09 fL) ($p>0.05$), this difference was not statistically significant. Microcytosis rate was higher in girls (9.7%) compared to boys (6.3%) ($\chi^2=6.14$; $P=0.013$).

Anemia data detected according to Hb<110 g/L are presented in Table IV and according to Hb<120 g/L in Table V. The lowest limit of MCV was 75 fL (70+ age in years). Anemia detected according to Dallman criterion is documented in Table VI.

Anemia detected according to simplified Dallman criteria is shown in Table VII.

The difference between the two evaluation criteria according to Hb or Hct is high ($p<0.001$) with Dallman criteria. It is known that a 3% difference occurs when automated

Table IIIb. Mean Values According to Age and Sex for 9.5-12 Years

	9.5-12 years				
	Mean	Boys	Girls		
N	583	287	296	t	p
Mean Hb (range)	12.40±0.91 (5.90-15.40)	12.49±0.86 (7.70-15.20)	12.3±0.95 (5.9-15.40)	2.49	0.013
Mean Hct % (range)	36.39±2.50 (20.90-48.50)	36.6±2.41 (24.7-46)	36.19±2.58 (20.9-48.5)	1.951	0.052
Mean MCV fL (range)	81.04±4.60 (57.10-93.00)	80.9±3.51 (57.6-88.7)	81.12±5.46 (57.1-93)	–0.412	0.68

Table IIIc. Mean Values According to Age and Sex for 12.5-16 Years

	9.5-12 years			
	Boys	Girls		
N	243	191	t	p
Mean Hb (range)	12.88±0.96 (9.5-17.10)	12.51±1.07 (6.70-15.4)	3.775	0.000
Mean Hct % (range)	37.681±2.67 (28.40-47.80)	36.82±2.74 (23.00-45.30)	3.290	0.001
Mean MCV fL (range)	82.05±4.29 (56.60-94.3)	82.76±5.34 (54.90-97.0)	1.552	0.121

Table IV. Data Evaluated According to WHO Criteria of Anemia for WIC[16] (women, infant and children)

	Hb<110 g/L	MCV<75 fL	Hct<33%	Hct+3<33%	Hb<110 g/L and MCV<75 fL
N	89	85	137	95	30
(%)	(5.8%)	(5.6%)	(8.9%)	(5.9%)	(2%)

Table V. Data Evaluated According to Different WHO Criteria of Anemia

	Hb<120 g/L	MCV<75 fL	Hct<36%	Hct+3<36%	Hct<38%	Hct+3<38%	<120 g/L and MCV<75 fL
N	497	85	709	490	1175	932	58
(%)	31.4%	5.6%	44.8%	31%	74.2%	58.9%	3.7%

Table VI. Values According to Classical Dallman Criteria

	Total 1531	Boys 798	Girls 733	χ^2	p	6-9 years 514	9.5-12 years 583	12.5-16 years 434	χ^2	p
Pathologic Hb values	423 (27.6%)	219 (27.4%)	204 (27.8%)	0.02	0.86	144 (28%)	162 (27.8%)	117 (27%)	0.14	0.93
Pathologic Hct values	625 (40.8%)	306 (38.3%)	319 (43.5%)	4.23	0.04	251 (48.8%)	253 (43.4%)	121 (27.9%)	45.34	0.001
After Hct +3 Pathologic Hct values	418 (27.3%)	204 (25.6%)	214 (29.2%)	2.53	0.11	161 (31.3%)	161 (27.6%)	96 (22.1%)	10.08	0.006

Table VII. Data According to Simplified Criteria of Dallman (y: years)

	Hct<35 for 6-11 y Hct<36>11 y girls Hct<37>11 y boys	MCV<77 for 6-11 y MCV<78>11 y girls MCV<78>11 y boys
Hct (%)	471 (29.8%)	94 (5.9%)
Hct+3	342 (22.3%)	

and spun Hct values are compared[15]. The ratio of anemic patients decreased to 27.3% when 3% Hct values were added to the students' data to correct for the technique used, which was quite similar to the anemic patients' ratio with Hb values (Table VI).

The data which were evaluated were found to be relevant especially with simplified Dallman criteria and when a 3% increase in Hct was made (with an accuracy of 96.5% and 95%, respectively). The accuracies of the different methods are documented in Table VIII.

optimum for oxygen transport would be a true form of anemia. But this is not easy to detect. Two diagnostic tests, Hb concentration and Hct, are available for anemia screening[15-21]. Whereas the World Health Organization differentiated cut-off criteria for Hb by age, sex, and physiological status[3], it established a single and universal cut-off point of <33% when using Hct for WIC (women, infant and children)[16]. Hct values are closely related with the blood taken by capillary or venous route and the technique used. Numerous studies have shown that capillary Hct is significantly higher than the venous value, a difference even more apparent in neonates[22]. Automated cell counters, which calculate the Hct from direct measurements of the mean cell volume, red cell number and the Hb, show slightly lower values than the Hct determined by a microcentrifuge[15]. The manual Hct is performed by an application of centrifugal force on a column of blood, where the degree of erythrocyte packing is optimal rather than complete. Small pockets of plasma are trapped

Table VIII. Sensitivity, Specificity, Positive and Negative Predictive Values and Accuracies According to Dallman Criteria of Anemia

%	Hct+3 (Simplified Dallman)	Hb<11 g/dL	Hb<12 g/dl	Hct<33%	Hct+3 <33%	Hct<36%	Hct+3 <36%	Hct<38%	Hct+3 <38%
Sensitivity	100	21	90.1	32.8	81.8	100	95.7	100	100
Specificity	95.2	100	89.5	100	100	73.9	91.9	32	53.8
Positive predictive values	88.7	100	76.7	100	100	59	81.6	35.6	44.8
Negative predictive vlaues	100	76.8	95.9	79.8	93.6	100	98.3	100	100
Accuracy	96.5	78.2	92.4	81.6	95	81	92.9	50.6	56.4

Discussion

Nutritional anemia is a widespread problem in children in developed and developing countries[1]. However, intercountry comparisons are unreliable because of non-uniform diagnostic criteria across surveys. Having any level of circulating red cells below the body

in the spaces between incompletely packed erythrocytes, which is estimated to be 3% under most conditions[15]. A (3%) correction factor is applied while calculating the Hct. In these settings, Hb value that is measured directly is more reliable and more closely related to the oxygen carrying capacity. The hypoxic effect of

high altitude is also another parameter that must be taken into account while Hb and Hct values are evaluated. For regions in which the population is dispersed over a variety of altitudes from coastal to mountainous locations, differences in ambient oxygen tension and erythropoietic stimulus do not permit a uniform diagnostic criterion for Hct or Hb[23,24]. As İstanbul is a coastal city, the alterations due to altitude were not taken into account in this study.

Besides the presence of all these handicaps, the Hct is an immediate and inexpensive test, requiring a minimal blood sample, and would have many advantages in nutritional assessment, if we could refine our approaches to its diagnostic use. The ratio of anemic children according to Hb and Hct criteria of classical Dallman in our study was 27.6% and 40.8%, respectively. The Hct values obtained after the addition of 3% were reevaluated again with Dallman criteria and the ratio of anemic children was 27.3%, which is quite similar to the values with Hb. We recommend 3% addition if cell counters are used for Hct variables, otherwise reference ranges serve improper interpretation of laboratory results.

More fundamentally, however, the conventional approach to the definition of anemia is as an end-stage process. If, however, a sufficiently firm and fixed predictive cut-off degree existed, it would greatly strengthen the value of surveys, but there are great variabilities in childhood cut-off levels according to age and gender.

In studies from different parts of the world, investigators choose to use a practical and generous cut-off of 38%[25]. Khusun's study[26] from Indonesia used the cut-off values of <12 g/dl to define anemia.

If we had used the cut-off criterion of the WHO (33%) or Hb 11 g/dl, we would have estimated that İstanbul school children have an anemia prevalence of less than 6%, and thus would assume this as a minimal public health problem. We found anemia in 22.3% of the school children with cut-off values according to simplified criteria of Dallman. This value is higher than that of other recent studies from Turkey. Koç et al.[27] found anemia in 7.8% of schoolchildren in the same age group (6-16) from the southeast region of Turkey using simplified criteria of Dallman. Aydınok et al.[28] reported a decrease in at least one of the hematological data (Hb, Hct, MCH, MCV) compared with their reference values (Hct 34%) for 13-14 years; Hct 35% for girls and 39% for boys 15-18 years; and for 13-14 years 12 g/dl for girls and 12.5 g/dl for boys and for 15-18 years 12 g/dl for girls and 13 g/dl for boys) in 12% of adolescents in the western region of Turkey[28].

In conclusion, an empirically chosen criterion of <35% Hct, MCV<77fL for 6-11 year olds, and Hct<36%, MCV<78 fL for girls aged 12-16 years and Hct<37%, MCV<78fL for boys aged 12-16 years will give more accurate results to define anemia.

We recommend the addition of a correction factor of 3% to counter data of Hct before the use of cut-off criteria to define and identify anemia with quality-assurance.

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