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Assessment of Mean Corpuscular Volume as a Surrogate Marker for Detecting Early Iron Deficiency among School Children

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Abstract

Background: The aim of the present study was to assess the mean corpuscular volume (MCV) as a surrogate marker for detecting early iron deficiency prior to definitive investigation and treatment.

Materials and Methods: This study was done on one hundred students in Swada Preparatory School – Sharkia Governorate from 2010 to 2011. They were subdivided into three groups: Group (A): comprised of 31 anemic children. Group (B): comprised of 19 microcytic children. Group (C): comprised the control group of 50 apparently healthy children with normal CBC. All subjects were subjected to: full history taking, thorough clinical examination and iron studies including: serum iron , total iron binding capacity, serum ferritin and transferrin saturation.

Results: There was a significant difference among studied subjects in height, presence of anorexia and pallor. Moreover, there was a significant difference among studied subjects in Hb, RBCs count, MCH, RDW ($p < 0.001$) and WBCs count ($p= 0.004$). We noticed a significant positive correlation between MCV (fl) and serum iron (mg/dl) in anemic subjects. Also there was a significant positive correlation between MCV (fl) and TIBC (µg/dl) in anemic subjects as well as a significant positive correlation between MCV (fl) and serum ferritin (µg/dl). In microcytic subjects, we found a significant positive correlation between MCV (fl) and iron (mg/dl) and a significant positive correlation between MCV (fl) and ferritin (µg/dl).

Conclusion: Every child with clinical manifestations of anemia proved by CBC who have microcytosis and low MCV should undergo iron studies (serum iron, serum ferritin, total iron binding capacity and transferrin saturation).

Keywords: Iron deficiency , anemia, children.

Introduction

Iron-deficiency anemia in children is an important problem worldwide, estimated to affect some 43% of the world's children[1]. Infants and young children have a high risk for developing iron deficiency (ID) because they have high demand for iron during the period of rapid growth. This is aggravated by the insufficiency of iron in their diet[2].

The first stage of developing ID is the diminishing of stored iron (pre-latent iron deficiency) characterized by reduced plasma ferritin concentration. When iron stores are almost empty, a latent iron deficiency will develop which may lead to the manifestation of Irin deficiency anemia (IDA)[3].

Ferritin is a complex of iron and the bind¬ing protein apoferritin. Ferritin reflects true iron stores and is not susceptible to the short-term variations that occur with serum iron levels and TIBC. However, ferritin is also an acute phase reactant and can be elevated with liver disease, malignancy, and chronic renal diseases[4,5]. Iron deficiency anemia is still probable if the serum iron level and transferrin satu¬ration are decreased and TIBC is increased. On the other hand, if the serum iron level is decreased and the TIBC and transferrin satu¬ration are decreased or normal, anemia caused by chronic disease is most likely[6,7].

Microcytosis is defined as the mean corpuscular volume of <74 fl based on the lower limit for the mean cell volume reference range (mean (2 SD)) defined by Isaacs et al. in a study of European children[8]. It was recognized that this cut off value would include a small number of normal, mainly young children, as the mean cell volume and hemoglobin concentrations increase slightly during early childhood [9].

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The aim of the present study was to evaluate the importance of mean corpuscular volume (MCV) as a surrogate marker for detecting early iron deficiency in school children.

Materials and Methods

This study was performed on one hundred students in Swada Preparatory School – Sharkia Governorate. The sample (two classes) were choosen randumly from seconed and third grades (one class from each grade) after the consent of school and Swada healthy unit from 2010 to 2011. Exclusion criteria was a history of anemia within the previous 12 months and known hematological abnormalities such as hemoglobinopathy.

Participants were subdivided into three groups: Group (A): comprised of 31 anemic children aging from 14 to 15 years old with mean age of 14.3 ±0.5 years. Group (B) : comprised of 19 microcytic children ranging from 14 to 15 years old, with mean age of 14.6 ± 0.5 years. Group (C): comprised the control group of 50 apparently healthy children with normal CBC and their age ranged from 14 to 15 years with mean age of 14.5 ± 0.5 years. All subjects were subjected to the folllowing:

(I) Full history taking stressing on age, sex, onset and duration of anemia, manifestations of iron deficiency anemia including anorexia, pallor, palpitation, headache, fainting, growth failure, pica and loss of memory and concentration.

(II) Thorough Clinical examination, measurment of weight (Kg), height (cm) and body mass index (BMI).

(III) Laboratory investigations including:

A- Complete blood count using electronic cell counter (Gen S system 2).

B- Serum iron and total iron binding capacity using (Automatic analyzer 917 Hitachi).

C- Serum ferritin using (elecyss 2010 Hitachi Roche).

D-Transferrin saturation using (TS = (serum iron / T.I.B.C) × 100).

Table1: Demographic and clinical data among studied groups.

		Group (A) N = 31		Group (B) N = 12		Group (C) N = 50		F	P
Age (years)									
	¯X±SD	14.3±0.5		14.6±0.5		14.5±0.5		2.15	0.12
	Range	14-15		14-15		14-15			
Wt (kg)									
	¯X±SD	55.4±10.1		57±8.1		55.5±9.1		0.21	0.8
	Range	42-90		46-72		43-75			
Ht (cm)									
	¯X±SD	148±		156±8		157±936		13.3	<0.001*
	Range	140-164		141-172		139-174			
BMI									
	¯X±SD	25.1±3.1		23.3±.9		22.7±5.3		2.85	0.06
	Range	21-33		16-32		15-34			
Gender								X^2	P
	Male	12	38.7	14	73.7	24	48.0	5.9	0.051
	Female	19	61.3	5	26.3	26	52.0		
Anorexia									
	- ve	*19	61.3	17	89.5	50	100.0	24.05	0.001*
	+ ve	12	38.7	2	10.5	0	0.0		
Pallor									
	- ve	*7	22.6	17	89.5	50	100.0	62.5	0.001*
	+ ve	24	77.4	2	10.5	0	0.0		

***p<0.05 Significant**

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Procedures:

Blood samples (about 5-6 cc) were obtained by vein-puncture, and divided into 2 parts; one part was collected in EDAT tubes (Ethylene-diamine-tetra-acetic acid) for complete blood count assay, the other tubes were plain sterile tubes without additives for serum iron, total iron binding capacity, serum ferritin and transferrin saturation tests. Samples for complete blood count were subjected to immediate assay, while samples for the other laboratory investigations were left for complete clotting, after which they were centrifugated and the separated serum was frozen at -20oC till the time of assay.

(I) Complete blood count (CBC) was performed for all patients and controls with determination of different indices as haemoglobin (Hb%) in mg\ dl, mean corpuscular volume (MCV) in fl, mean corpuscular hemoglobin (MCH) in pg, mean corpuscular hemoglobin concentration (MCHC) in g/dl and hematocrite percent (HCT %).

(II) Serum iron and total iron binding capacity

Table2: Findings of complete blood picture and iron studies among the studied participants.

	Group (A) N = 31	Group (B) N = 12	Group (C) N = 50	F	P
HB(g/dl)					
¯X±SD	*9.7±0.8	12.6±1.7	12.8±1.5	53.1	0.001*
Range	7.8-11.3	10.2-16.3	11-18.2		
RBC(x10³)					
¯X±SD	*3.5±0.4	4.95±0.6	4.4±0.7	38.3	0.001*
Range	2.8-4.6	3.6-5.8	3.2-6.2		
Iron(mg/dl)					
¯X±SD	67±25	79±25.1	85.3±8	1.86	0.16
Range	23-117	38-118	78-94		
TIBC(µg/dl)					
¯X±SD	304.1±82	285.6±67	362.3±46	1.39	0.25
Range	179-488	187-411	309-392		
Transferrin.					
¯X±SD	277±72	307±74	324±32	1.37	0.26
Range	169-442	197-441	292-354		
Ferritin(µg/dl)					
¯X±SD	144.9±98	210±105	169±58	2.53	0.08
Range	17.7-288	19.7±313	103-222		
Median	193	257	178		
WBC					
¯X±SD	5.6±2.2	7.2±2.2	7.2±1.98	5.7	0.004*
Range	3.1-11.2	4-11.7	4.5-13.8		
MCV(fl)					
¯X±SD	75.1±2.2	80±4.3	84.8±3.86	72.6	0.001*
Range	70-79	71.1-89	80-94		
MCH(pg)					
¯X±SD	*23.8±1.4	+26.6±1.0	28.8±1.3	72.1	0.001*
Range	22-28	25-28	26-33		
RDW(%)					
¯X±SD	13.3±0.4	15.2±1.5	13.7±0.4	24.8	0.001*
Range	12.2-14.3	13.1-17	13.3-14.1		

***p<0.05 significant**

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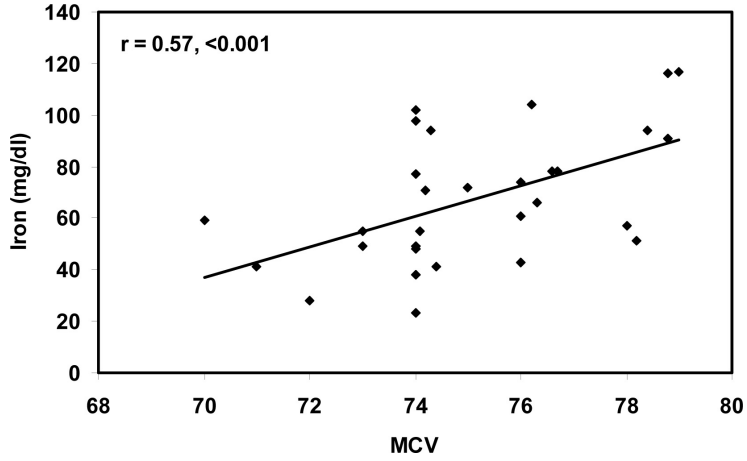


Figure 1: Shows a significant positive correlation between MCV(fl) and serum iron (mg/dl) in anemic subjects.

(TIBC) were evaluated for patients and controls. Reference values in children were 50-120µg/dl for serum iron and210-430µg/dl for TIBC;.

(III) Serum ferritin was evaluated in patients and controls. Reference value for children was (7-140µg/dl)[10].

Interpretation of results:

Patients who fulfilled Hb <11g/dl. and also had 2 of the following 3 criteria were diagnosed as iron deficiency anemia (IDA):

- MCV <77 fl.
- Serum transferrin saturation (TS) <16% (TS= serum iron x 100/ serum total iron binding capacity).
- Serum ferritin <12ng/ml.[11]

Data analysis:

Patients data were tabulated and statistical analysis was performed using Microsoft Excel version 6.0 and the statistical package for social science (SPSS) version 11.0. The following methods were employed: Frequency distributions and percent distributions,Mean, standard deviation and range for numerical data,Comparison of means to assess statistical significance of difference using T test,Comparison of distributions of descriptive data using Chi-Square test,Correlation between numerical data. The obtained correlation coefficients (r values) were tested for significance, and correlation results were expressed as either positive, negative and non-significant.

Results:

Table (1) shows demographic and clinical data among studied groups: there was a high significant difference among studied subjects in height, presence of anorexia and pallor.

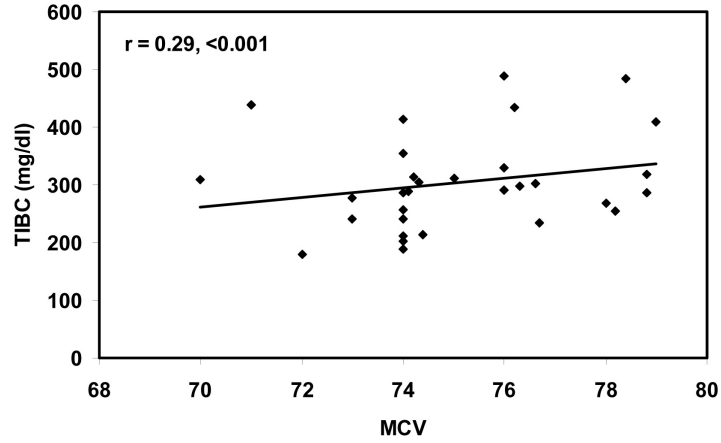


Figure2: Shows a significant positive correlation between MCV (fl) and TIBC (µg/dl) in anemic subjects.

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Table (2) shows findings of complete blood and iron studies in the studied subjects: there was a significant difference among studied subjects ($p < 0.001$) in Hb (g/dl), RBCs count, MCH (pg), RDW(%) and also a significant difference among them regarding WBCs count ($p= 0.004$).

Figure 1 shows a significant positive correlation between MCV(fl) and serum iron (mg/dl) in anemic subjects, figure 2 shows a significant positive correlation between MCV(fl) and TIBC (µg/dl) in anemic subjects, figure 3 shows a significant positive correlation between MCV (fl) and serum ferritin (µg/dl) of anemic subjects, figure 4 shows a significant positive correlation between MCV(fl) and iron (mg/dl) of microcytic subjects and figure 5 shows a significant positive correlation between MCV(fl) and ferritin (µg/dl) of microcytic subjects.

Discussion:

The diagnosis of ID and mild IDA relies heavily on identifying mature red blood cells (RBC) with low MCV, low MCH, and increased RDW. Hemoglobin level of <110 g/L is strong but late predictor of ID. Standard biochemical markers of iron metabolism are serum Fe, transferrin, transferrin saturation, ferritin, and soluble Tf receptors [12].

The first stage of developing ID is the diminishing of storage iron (pre-latent iron deficiency) seen by reduced plasma ferritin concentration. When iron stores are almost empty, a latent iron deficiency will develop which may lead to the manifestation of IDA[3].

This was against the present study findings as there was no significant difference between studied groups regarding serum ferritin, although it showed lowest values in anemic subjects (144.9±98µg/dl), when compared with those having microcytosis and the control group (210±105 µg/dl, and 169±58 µg/dl respectively).

Also, there was a significant difference among studied subjects regarding Hb content and RBCs count with lowest values found in anemic subjects (9.7±0.8 g/dl and 3.5±0.4 $x10^3$ respectively).

Typically, simple screens are defined as either low hematocrit levels or low hemoglobin levels. Because abnormal thresholds for these 2 indices are not uniform in the literature, we chose 3 different criteria for this study, as follows: hematocrit level of <33%, hemoglobin level of <11 g/dL, and hemoglobin level of <10.5 g/dl [13,14].

On the other hand, we found lowest MCV values in anemic group (75.1±2.2 fl) when compared with microcytosis and control group (80±4.3 fl, 84.8±3.86 fl).

Microcytosis is characterized by low MCV and elevated RDW. The Mentzer index (MCV divided by red blood cell count) is used to differentiate microcytic anemia. Different studies have sugested 3 different criteria for microcytosis, as follows: MCV of <70 um3 and RDW of >14%; MCV of <70 um3 and RDW of >14.5%; and MCV of <70 um3, RDW of >14.5%, and Mentzer index of >13 [14,15].

A study by Pusic et al. also looked at detection and follow-up rates of microcytosis, in all children aged 6–36 months presenting to a pediatric emergency department. Over a four month period, 8% of children had a low MCV with no previously identified explanation [16].

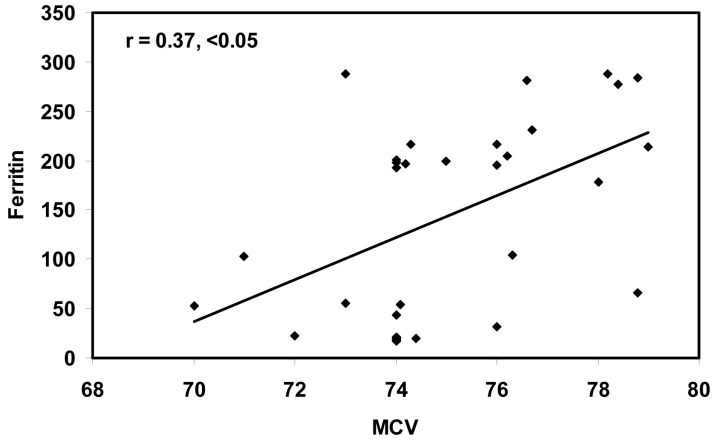


Figure3: Shows a significant positive correlation between MCV (fl) and serum ferritin (µg/dl) among anemic subjects.

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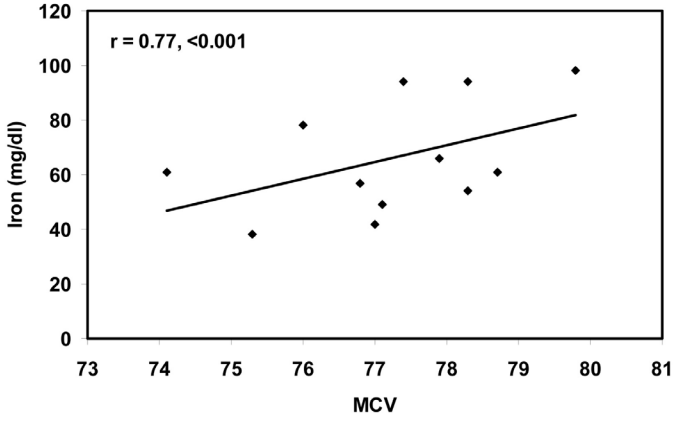


Figure4: Shows a significant positive correlation between MCV (fl) and iron (mg/dl) in microcytic subjects.

After confirmation of microcytosis on CBC, physicians should first order a serum ferritin level. If the ferritin level is consistent with iron deficiency anemia, identifying the underlying cause of the anemia is the priority [17].

We found that there was no significant difference among studied subjects gender. This was against Thorsdottir et al. findings who indicated the gender apparently playing an important role in infant's iron status [18]. Moreover, Vendt et al. found that boys had a tendency to have lower ferritin concentration than girls, but the difference was not statistically significant [19].

In all study groups, we found that the number of males was more than females, but the difference was not significant while Brooker et al. found that in general, females are more anemic than males especially in the reproductive age due to physiological variations. Also a study among Kenyan preschool children reported that the prevalence of anemia and IDA was significantly higher in males than females and the prevalence decreased steadily with increasing age [20]. A similar observation was also reported among Zanzibar school children[21]. In Malaysia, Khor et al [22] reported that the prevalence of anemia was significantly decreased with age.

We found that there was a significant difference in the presence of pallor and anorexia (more in anemic subjects). This agreed with Muhe et al. who found that as the severity of anemia increases, physical findings may include a systolic murmur and pallor of the mucous membranes, nail beds, and palmar creases [23].

In our study there was significantly more anorexia (38.7%) in anemic group and (10.5%) in microcytic group. This finding agreed with those of Couper and Simmer [24]. Wright et al. reinforced the importance of a low hemoglobin and, unexpected MCH, as specific markers of iron deficiency in this age group. However, these are still insensitive, as each only identified half the children who showed a substantial treatment response. The MCV and Zinc protoporphyrin (ZPP) were much less specific, but when both were abnormal these also produced a substantial therapeutic response, even if the hemoglobin and MCH were within normal limits[25].

Our study showed a significant difference between the studied groups considering the HGB, RBCs, MCV and MCH. Student t-test showed a significant difference between means of all parameters (p-value 0.001), and a significant difference for WBCs between cases and controls (p-value 0.004). This finding agreed with Ferrara, et al.[26] findings.

In the present study, TIBC level was lower in the anemic group than in controls and microcytic groups, however, this was statistically insignificant between the two groups studied which agreed with Ferrara, et al. findings (26). Gregory found that ferritin correlated only weakly with the other markers probably because of its strong tendency to rise in the presence of any infection. Zinc protoporphyrin is not often used clinically and initially seemed highly non-specific [27].

Conclusion

Every child with clinical manifestations of anemia proved by CBC who have microcytosis and low MCV

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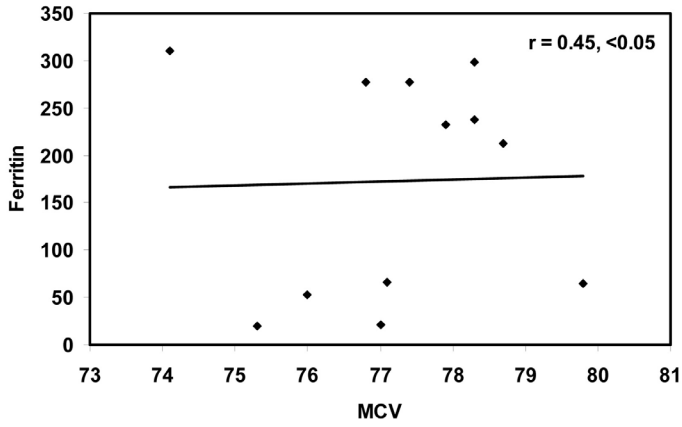


Figure5: Shows a significant positive correlation between MCV (fl) and ferritin (µg/dl) of microcytic subjects.

should undergo iron studies (serum iron, serum ferritin, total iron binding capacity and transferrin saturation).

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