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# Does the Mean Corpuscular Volume Help Physicians Evaluate Hospitalized Patients with Anemia?

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***Abstract:*** *The authors analyzed the value of using mean corpuscular volume (MCV) as a guide for selecting tests for further evaluation of anemia in hospitalized patients. Of the 2,082 Patients with anemia admitted to the medical service of a teaching over one year.655 (31% Bad further diagnostic tests to evaluate the cause of the anemia. Within this group of 655 Patients, 399(61%) bad normal MCVs. Over half the patients with abnormal serum vitamin B12. 12 folate, or ferritin levels, or with low serum iron (Fe) levels with elevated total iron-binding capacity (TIBC), did not have the MCVs expected according to the classification of anemia proposed. By Wintrobe. Furthermore, 5% of patients with evidence of iron deficiency bad big MCVs, and about 12% of patients witb decreased vitaminB12 Levels bad low MCVs.*

*The MCV was quite. Specific in identifying patients who bad low ferritin levels: specificity was 85 %.,however, sensitivity was only 48% tge MCV was also specific 88% for identifying patients who bad low Fe with elevated TIBC, however, sensitivity was only 43%. The MCV was poor in identifying. Patients with abnormalities of serum vitamin B12 and folate Levels. In this, study the MCV. Did not provide sufficient diagnostic accuracy to be a useful criterion for the selection of more definitive tests in the evaluation of anemia in hospitalized patients.*

***Key Words:*** *Animal, decision, making, diagnostic tests, mean corpuscular volume.*

## 1. INTRODUCTION:

THE ERYTHOCYTIC INDICES first described by Wintrobe in 1930. became the basis of his commonly used classification of anemia. Current teaching continues to recommend that anemia be evaluated on the basis of red blood cell size., determination of which has been greatly facilitated by the introduction of electronic particle counters . 2 for patients with small red blood cells( low MCV) ,studies of iron metabolism are recommend-Ed.for patients with large red blood cells ( high MCV) ,studies for vitamin B12 or folate deficiency are recommended ,3-7.

The MCV is frequently ignored and that the cause of a patients anemia is seldom evaluated in this traditional manner.8 Frequently, to save time, the house staff orders multiple tests for each patient .9. The discordance between teaching and practice stimulated us to investigate the usefulness of the MCV in the die-gnosis of anemia in hospitalized patients on the medical service of a teaching Hospital. Received from the department of Medicine, the Division of General Medicine. Gamhoryat Hospital, and the center for Clinical computing, Harvard Medical school (CS)., the Division Of Hematology-Oncology, Gamhoryat Hospital.

## 2. METHODS:

Using clinQuery, 10 a program to search the computerized clinical database at Gamhoryat hospital In Kabul, the electronic medical recards of 15.283 Adult patients who WERE ADMITTED FROM July 1,.2010,through June 30, 1986 Were analyzed. Anemia was defined as a hematoctit of Less than 42% in men and Lessthen 36% hn women, according to the first complete blood count in a sample Drawn within 48 hours of admission . (The findings in this study were unchanged When a more stringent cutoff hematocrit of 31% was used.) of the 14,215patients 6,316 (41%) were anemic. Of 5,596 patients admitted to the medical servic3,092 (38%) were anemic on their first admission during the period of study. Of these 2,082 patients ,655 (31% ) had laboratory evaluation of their anemia. These 705 Patients, of whom 45% were male and 55 % were female, formed our study population. The mean age (- + SE) was 69.2 -+ = 0.7 Years and did not differ between men and women. The mean hematocrit on admission was 31.7 – 0.2% and did not differ between men and women.

The MCV was measured by either a Coulter S or Coulter S plus particle coulter (coulter Electronic, 590 W west 20th. Hialeah, FL33010) using electronic impedance technology. The normal range at Gamhoryat , Hospital is 80 to 96 fl. Table 1 shows the Distribution of MCVs for 705 patients in our study group who had laboratory evaluation of their anemia and for the larger population of patients on the medical service who had anemia, but did not have additional diagnostic tests a somewhat greater proportion of patients with microcytosis or macrocytosis. As compared with patients with normocytic indices, had further diagnostic evaluation, introducing a small selection bias into the study population.

The red blood cell distribution width (RDW), although calculated by the auto analyzers, was not recorded in the hospitals computer.

| | **Table 1: Evaluation of ANEMIA** | | | | |
|---|---|---|---|---|---|
| | Distributing if Mean corpuscular Volumes (MCVs) in2, 082 Medical | | | | |
| | Patients with Anemia | | | | |
| | Patients with | | | | |
| | Further | | Patients without | | |
| | Diagnostic Tests | | Further | | |
| | (Study population) | | Diagnostic Tests | | |
| | MCV(f1) | No | (%) | No | (%) |
| | <80 | 101 | (14) | 61 | (4) |
| | 80 to 96 | 425 | (61) | 1,140 | (80) |
| | >96 | 180 | (25) | 226 | (16) |
| TOTAL | | 705 | (100) | 1,427 | (100) |

| **TABLE 2 : Results of Diagnostic tests in patients with Anemia** | | | |
|---|---|---|---|
| Total patients | | patients with | |
| Having Each | | Abnormal | |
| Diagnostic Test | | Test Results | |
| Test | No | No | (%) |
| Bone marrow | 78 | 53 | 68 |
| Ferritin | 203 | 25 | 12 |
| Fe/TiBct | 505 | 81 | 1 |
| Vitamin B12 | 298 | 18 | 6 |
| Folate | 276 | 11 | 4 |

- Abnormal Values Are Bas follows: ferritin <15 ng/ml.Fe< 50
- Mg/di and TIBC < =350 miu g/di> vitaminB12 <171 pg/ml> folate<2.6
- ng/ml.

Laboratory evaluation of anemia included measurement of serum vitamin B12 (n+298),serum Folate (n=276) ,and serum ferritin (n=203),all measured by radioimmunoassay., and total iron(Fe) Derived from colorimetric methods, AND total iron-binding capacity (TIBC ),derived by transferrin Immunoassay, n=505)., and bone marrow analysis (n=78) (tABLE2) Serum vitamin B12 levels below 171 pg/ml and serum folate levels below 2.6 ng/ml are considered abnormal at Gamhoryat Hospital Kabul.

We defined iron studies highly Suggestive of iron deficiency as those indicating an Fe below 50 mio gram/dl with a Simultaneous TIBC above 350 moil gram/dl. Serum Ferritin levels 15 ng/ml ar consid.

| **TABLE 3: Distribution of Mean Corpuscular Volumes (MCVs) in655 patients with Anemia who had further Diagnostic Tests.** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Ferritin | | Fe/TIBC* | | VitaminB12 | | Folate | |
| MCV(fl) | No | (%) | No | (%) | No | (%) | No | (%) |
| <80 | 60 | (21) | 86 | (17) | 18 | (6) | 16 | (6) |
| 80 to 96 | 165 | (65) | 341 | (68) | 144 | (48) | 136 | (49) |
| >96 | 48 | (14) | 78 | (15) | 136 | (46) | 124 | (45) |
| TOTAL | 290 | (100) | 505 | (100) | 298 | (100) | 276 | (100) |

*iron/ total iron-binding capacity. Thyroxin level below 4 miu gram/dl (n=14) or a thyroid stimulating hormone level above 7mIu/ml (n=24) ., 4)a discharge diagnosis of cancer (n=103) (the latter to exclude patients with possible chemotherapy-in du- Ced macrocytosis ).,or5) a serum glucose level above140mg/dl (n=180), which may increase cell size in electro- Nick cell counters as result of hyper osmolality of the erythrocytes. 20 We also performed the foregoing analysis a By excluding patients with known causes of normochromic normocytic anemias:1) renal disease a serum crea- Tinnier level above 2mg/dl (n=120) or discharge diagnosis of renal disease (n=86),2) chronic infectious ,

Inflammatory or neoplastic disease, as outlined above. or3) acute gastrointestinal bleeding (n=95).Some of The 705 patients in our study group had more than one of the above conditions or laboratory abnormalities., However, in our analysis we excluded each group individually.

**3. RESULTS:**

Among the 91 patients with microcytosis (Table1), physicians ordered measurement of Fe and TIBC level for 86(95%) and measurement of vitamin B12 levels for18 (20%) (Table3 ). Among the165 patients with Macrocytosis, physicians ordered measurement of vitamin B12 levels for 136 (82%) ,and Fe and TIBC level for 78 (47) .Thus, to some extent, the house staff did use the MCV as a criterion for selecting tests in the evaluation of anemia. Over half these diagnostic tests, however ,were ordered for the 399 patients with normocytic indices.

The sensitivity and specificity of the MCV for detecting a low Fe with an elevated TIBC, allow ferritin level allow B12 level, or a low folate level are shown enables 4 through 6 . Thaws two test characteristics are calculated for a range of MCV values., the laboratory-defined cutoff for an abnormal MCV (<80fl or>96fl.) is identified by an asterisk on each table. According to these criteria ,the MCV was most useful in identifying patients with abnormal results on iron studies. The MCV had an83% specificity and a 48% sensitivity for low ferritin levels. Similarly, the MCV had an88%% specificity, but only a43% sensitivity, for a low Fe with an elevated TIBC. when MCVs less than 84 fl, rather than 80 fl were considered abnormal, the specificity decreased to 81% and the sensitivity increased moderately to54% (Table 4). Five percent of patients with allow Fe and an elevated TIBC had an MCV above 96 fl. While 52% of patients with low ferritin levels had normal MCVs None had a high MCV.the MCV identified patients with low vitamin B12 levels with only 55% specificity and 61 % Sensitivity (Table 6). The MCV identified patients with low folate levels with only 55% specificity and 36% Sensitivity (Table 7).Twelve percent of patients who had allow vitamin B12 level and 9% of patients with allow Folate level had an MCV less.

**TABLE 4: Test characteristics of Mean Corpuscular Volume (MCV) in the Evaluation of Anemia: predicting LOW iron (Fe With Elevated Total iron-binding Capacity (TIBC)**

| | Sensitivity | | Specificity | |
|---|---|---|---|---|
| MCV (f1) | (%) | (No) | (%) | (No) |
| <70 | 19 | (15/81) | 98 | (415/424 ) |
| <76 | 32 | (26/81) | 94 | (397/ 424) |
| <80 | 43 | (35/81) | 88 | (373/424 ) |
| <84 | 54 | (44/81) | 81 | (344/424) |
| <92 | 85 | (70/81) | 45 | (191/424) |

**TABLE 5: Test characteristics if Mean Corpuscular Volume (MCV) in Predicting Low Ferritin.**

| | | Sensitivity | | Specificity |
|---|---|---|---|---|
| MCV((fl) | % | (No) | % | (No) |
| <70 | 24 | (6/25) | 96 | (171/178) |
| <76 | 36 | (9/25) | 90 | (161/178) |
| <80* | 48 | (12/25) | 83 | (147/178) |
| <84 | 60 | (15/25) | 74 | (131/178) |
| <92 | 88 | (22/25) | 39 | (70/178) |
| <96 | 100 | (25/25) | 16 | (29/178) |
| Lower limit of normal in this laboratory. | | | | |

**Table 6: Test characteristics of mean corpuscular volume (MCV) in the (MCV) in the evaluation of anemia: Predicting L low serum flote.**

| | | Sensitivity | | Specificity |
|---|---|---|---|---|
| MCV(fl) | % | (No) | % | (No) |
| >105 | 18 | (2/11) | 86 | (228/265) |
| >100 | 27 | (3/11) | 69 | (182/265) |
| >96* | 36 | (4/11) | 55 | (145/265) |
| >92 | 55 | (6/11) | 31 | (81/265) |
| >84 | 91 | (10/11) | 8 | (20/265) |

Seward et .al ., MCV iN EVALUATION of ANEMIA.

84 fl ,.No Patient had both a Low vitamin B12 Level and a low folate level. When only MCVs 105 fl. Or higher were considered abnormal, the MCV identified patients with low vitamin B 12 or folate level with about the same sensitivity and specificity as seen when low Mcvs predicted abnormalities in iron metabolism. With all four-laboratory measurements, Cutoffs at more and more abnormal MCVs became progressively more specific but also progressively less sensitive. For iron example, anMCV below 70 fl, was very specific for iron deficiency, as was an MCV of 105 fl, or higher for vitamin B12 or folate deficiency, although few patients with these laboratory abnormalities had abnormal MCVs.

These test characteristics did not substantially improve when the study group was subdivided into patients with a hematocrit of less then 32% and patients with a hematocrit of 32 or higher, or when the griup was subdivided into those who were under 70 Years of age and those who were 70 years old or older.

The sensitivity and specificity of the MCV did not improve when patients with conditions other than iron deficiency that might have deceased the MCV (infection, inflammation, cancer, thalassemia, or sideroblastic anemia) were excluded from the analysis. Similarly, these calculations did not improve when condhtions other than vitamin B12 or folate deficiency that might have increased the MCV (reticulocytosis, liver disease, alcoholism

Hypothyroidism, hyperglycemia, or chemotherapy) were excluded from the analysis, the test characteristics also did not change when patients with known causes of normochromic, normocytic. Mias were excluded.

**4. DISCUSSION:**

These findings show a poor correlation between the MCV and expected test results in the evaluation of anemia in hospitalized patients. More than half the patients whose tests reflected a deficiency of iron, vitamin B12 or folate did not have the MCVs expected for these disorders, and these deficiency states would have been missed if the MCV had been the criterion for ordering these tests.in addition to demonstrating that a normal MCV does not exclude iron, vitamin B12, or folate deficiency, these findings show that a high MCV does not rule out possible iron deficiency, and a low MCV does not rule out vitamin BB12 or folate deficiency.

Others have reported that the MCV is an imperfect guide in the evaluation of anemia. It is estimated that about 30% of patients with iron-deficiency anemia have normocytic indices.21 Moreover, others have explained vitamin B12 and folate-deficient anemia with non-macrocytic indicted on the basis of coincidental iron deficiency or Thalassemia or excessive erythrocyte fragmentation 5,22.24 Recent report, however, indicates that the MCV is normal in perhaps one-third of Patients who have pernicious anemia, typically those with little or no anemia. 25 none of these studies has shown the marked lack of sensitivity of the MCV in identifying patients with anemia due to these deficiency states that was found in the present study. This lack of sensitivity makes the MCV virtually useless a discriminator for ordering further or more specific tests for these hematologic conditions in large populations of anemia patients in an inpatient setting such as ours.

There are some limitations in study of this kind, notably that this was a retrospective study and that the precise cause of anemia could not be ascertained in each case. In this retrospective cohort analysis, patients were selected because diagnostic tests had been ordered to evaluate anemia .However, the physicians elected to order such tests for less than one-third of anemic patients, perhaps because the causes of anemia in the others were already apparent or because there were more pressing clinical concerns. It is also possible that the fact that most anemic patients had a normal MCV discouraged further evaluation (Table1). Since the RDW was not available for our analysis, we cannot speculate on its usefulness in conjunction with the MCV.finally, we did not evaluate the usefulness of the peripheral blood smear, which may yield additional clues to the cause of a patient's anemia.

Although low serum levels of vitamin B12 and ferritin clearly define deficiencies of this vitamin and of iron, the anemia in such patients could have been during small or large part to other factors. Nevertheless, it is on the Basis of such abnormal serum levels that still more definitive studies, such as marrow examination, a schilling test, or gastric analysis in the diagnosis of pernicious anemia, are undertaken. General internists usually consider allow serum ferritin or folate level sufficient to initiate diagnostic trial of therapy, although serum folate levels are a poor indicator of tissue stores.

Since patients in an acute care teaching hospital often have multiple medical problems that may contribute to anemia on a multifactorial basis, the data in this study were reevaluated after exclusion of different subgroups that might have skewed the results. This led to no improvement in the diagnostic value of the MCV did not improve when analysis was restricted to patients with severe anemia. On the positive side, allow MCV was shown to have a high specificity for abnormalities indicating iron deficiency. Since few healthy patients have low MCVs, few unnecessary iron studies would be ordered while strictly following the classic algorithm. On the other hand, allow MCV is not sensitive for iron abnormalities. Since most patients with these abnormalities have normal or even high MCVs, the classic algorithm markedly under diagnoses a common disease. The sensitivity of the MCV can be increased and more patients with disease can be identified, but the specificity will decrease and more tests will be performed in unaffected patients (Tables 4-And 5). An MCV of 105 fl, or higher yielded a sensitivity and specificity for detecting low serum levels of vitamin B12 or folate similar to those of a low MCV inpredicting abnormalities in iron metabolism (Tables 4and 6 ). These findings are similar to those of Jen et al. 26 In contrast are the conclusions of the study by Griner and Oranburg in which the probability of a low folate or vitamin B12 level among anemic hospitalized patients whose MCVs were not elevated was so low (0.1%) that assay of these vitamins was of little value. The Population in the study by Griner and Oranburg ,reported in 1978, had amarkedly different distribution of MCVs from that found among our patients. Perhaps this difference reflects a change in the types of patients who have been admitted to a cute care hospitals during the past decade. We can only speculate about why the classic algorithm performs so poorly in the evaluation of hospitalized patients with anemia . perhaps the clinical meaning of MCV has changed since the time of wintrobe.1 when MCVs were calculated by hand , hematologists may have carefully selected patients who Needed this time-consuming and labor-intensive test .Today, however, every patient who has a hematocrit measurement has an MCV determined as well. Another major factor in interpreting these findings is the increased severity of illness in patients currently hospitalized on acute care inpatient svaluations of pure anemia's, and one might anticipate that anemia in most hospitalized patients is related to the underlying condition that mandated admission to the hospital.previous studies have shown that the most common cause of anemia in hospitalized patients is the so-called ,,anemia of chronic disease.27,28 This may be the reason that the house staff ordered tests to evaluate the nature of the anemia in only one-third of all the anemic patients admitted to the medical service during the study period.

It would be of interest to do a similar analysis of the Value of the MCV in outpatients, in whom one would expect to encounter more frequent examples of anemia due to single, well-cricumscribed pathophysiologic disorders.

Clinical algorithms are an increasingly common part of the modern practice of medicine. 29The need for quality assurance and cost containment provides strong incentive to develop such an approach for common medical problems. These decision guides are frequently based on a review of the literature and expert consensus, but not on the analysis of a large body of clinical datd. We have found that, at least for ill patients admitted to a large teaching hospital IN t he current era, the classic algorithm for evaluating patients with anemia appears to be inadequate .

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