



INITIAL DIAGNOSIS AND IMPROVED CLASSIFICATION OF ANEMIA BY RED CELL DISTRIBUTION WIDTH AND MEAN CORPUSCULAR VOLUME FROM ITS ORAL MANIFESTATION.

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Abstract

Background/Purpose: Anemia is the most common hematological disorder around the globe. This study evaluated whether anemia patients had specific oral manifestations based on the classification by Mean Corpuscular Volume and Red Cell Volume Distribution Width

Methods: The hematological screening includes estimations of red blood count, hemoglobin %, mean corpuscular volume, mean corpuscular hemoglobin, hematocrit, red cell distribution width, ferritin, iron, total iron binding capacity, vitamin B12, liver function tests, and kidney function tests and anemia classified and matched with oral manifestation.

Results: In the study, the occurrence of oral signs and symptoms could not be correlated with the distribution of subjects because of the overlap of oral manifestations in different causes of anemia. The hemoglobin % was significant with a p-value of 0.001 which means that hemoglobin % has an important role in the occurrence of anemia. The Mean corpuscular volume in diseases was found to be statistically significant, with a p-value of 0.001 which means that it is necessary for the classification of different types of anemia. The standard deviation of red cell distribution width values in diseases was found to be statistically significant, with a p-value of 0.001 which means that it is important for the classification of different types of anemia.

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INTRODUCTION:

'Mouth is a mirror of the body, which reflects the systemic disease'-Sir, William Osler.

Anemia is a global problem, which is worst in developing countries. Anemia can be classified from three points of view: pathogenesis, red cell morphology, and clinical presentation. All are important to guide the diagnosis. The initial classification of anemia can be improved substantially by including RDW and histograms of red cell volume as these variables become part of the routine blood count. Red cell distribution width (RDW), a component of an electronic complete blood count, is a measure of heterogeneity in the size of circulating erythrocytes.^[1] The RDW is used as an auxiliary index to aid in the diagnosis of various types of anemia. The RDW can be very useful in distinguishing between different types of anemia, especially if more than one types of anemia are present. Oral mucosa reflects the general health status. Dentists can play an important role in the identification and thereby prevention of anemia, as oral manifestation is the earliest feature of the condition.^[2]

Anemia is classified by the size of red blood cells in the morphological approach; this is done either automatically or through microscopic examination of a peripheral blood smear. The mean corpuscular volume reflects the size (MCV). If the cells are smaller than normal (less than 80 ft), the anemia is microcytic; if they are normal (80-100 ft), the anemia is normocytic; and if they are larger than normal (more than 100 ft), the anemia is macrocytic.

The study was done to determine the type of anemia by evaluating the oral changes based on the classification of anemia by Mean Corpuscular Volume and Red Cell Volume Distribution Width, this can provide a rapid and useful guide in our daily practice.

MATERIALS AND METHOD

PARTICIPANTS:

The study population consisted of 30 subjects (10 male, 20 female) suffering from anemia with oral symptoms such as atrophic Glossitis, Glossodynia, Angular Cheilitis, Recurrent aphthous ulcer, and oral candidiasis, diffuse erythematous mucositis, pale oral mucosa attending the out-patient department were included. Pregnant patients were excluded from the study. Patients were diagnosed as having Iron deficiency anemia when men had hemoglobin < 13 g/dL, women had hemoglobin < 12 g/dL, and all of them had serum iron levels < 60

mg/dL according to the World Health Organization criteria. Patients with serum vitamin B12 levels < 200 pg/mL, or folic acid levels < 4 ng/mL were defined as having iron, vitamin B12, or folic acid deficiency, respectively. serum creatinine (i.e., men, >131 mM; women, >115 mM) concentrations indicative of renal dysfunction, serum bilirubin (Direct-0.2mg/dl, Indirect-0.2-1mg/dl), serum creatinine 0.6 -1.4 mg/dl, GGT (male-50 U/L, female -32U/L), SGPT (male-0-42 U/L, female -0-32U/L), SGOT value (Male 53-128U/L, female -42-98U/L) indicative of liver dysfunction. This study was approved by the institutional review board, informed consent was obtained from all the participants and the study protocol adhered to the tenets of the declaration of Helsinki (2013) (Ethical approval no KIDS/011/2021/11 dated 01/07/2021). Examination of the patients for oral signs and symptoms as per criteria were recorded in a specialized proforma with regard to the study using Dental Mouth Mirrors, Dental Explorer, and Williams Periodontal Probe. Blood sample of each subject was collected using the aseptic method.

BLOOD ANALYSIS

Collected blood samples were subjected to complete blood count estimation, serum ferritin, total iron binding capacity, iron, and estimation of serum B12 was estimated using direct chemiluminometric technology and Renal Function Test and Liver Function Test. Detailed medical histories of the subjects were taken before the clinical examination.

STATISTICAL ANALYSIS:

The differences in frequency of Hb, total iron binding capacity, iron, estimation of serum B12, Renal Function Test, and Liver Function Test were compared by the Chi-square test. Prevalence of mean corpuscular volume in diseases and Red Cell Distribution Width in disease using ANOVA test.

RESULT:

Iron deficiency anemia, in which 3(25.0%) were males and 9(75.0%) were females in Vitamin B12 deficiency - 3(27.3%) were males and 8(72.7%) were females and in anemia of chronic disease 4(57.1%) were males and 3(42.9%) were females. The results were not significant as the p-value was 0., hence sex doesn't influence the occurrence of anemia.

The results did not reveal any great significance, in the prevalence of different types of anemia among patients of different age groups. Since the result does not indicate any significant correlation (p -

0.89) in the age group of 24 - 70 years, it can be concluded that age doesn't influence the occurrence of anemia.

The study of the occurrence of oral signs and symptoms could not be correlated with the distribution of subjects because of the overlap of oral manifestations in different causes of anemia.

From this study it was found that the mean and standard deviation value of red blood count for Iron deficiency anemia is 3.92 and 0.59, for Vitamin B12 is 3.77 and 0.90, and for Anemia of chronic disease is 2.52 and 0.32.

The result had a p-value of 0.001 which is significant.

The hemoglobin % was significant with a p-value of 0.001 which means that hemoglobin % has an important role in the occurrence of anemia.

The Mean corpuscular volume in diseases was found to be statistically significant, with a p-value of 0.001 which means that it is necessary for the classification of different types of anemia.

The Mean corpuscular hemoglobin in diseases was found to be statistically significant, with a p-value of 0.001 which indicates that it influences the occurrence of anemia.

The hematocrit values in diseases were found to be statistically significant, with a p-value of 0.001 which denotes that it is related to different types of anemia.

The standard deviation of red cell distribution width values in diseases was found to be statistically significant, with a p-value of 0.001 which means that it is important for the classification of different types of anemia.

The Coefficient of variance of red cell distribution width values in diseases was found to be statistically significant, with a p-value of 0.001. This data indicates that there is a correlation between the prevalence of Coefficient of variance of red cell distribution width in anemic subjects.

The mean and standard deviation value for Ferritin is 9.98 and 9.32, for serum iron is 120.29 and 69.07 and Total iron binding capacity is 461.25 and 78.11 which means that it is classified as iron deficiency anemia with low mean corpuscular volume and high red cell distribution width.

The mean and standard deviation value for vitamin B12 is 175.10 and 33.68

which means that it is classified as Vitamin B12

deficiency with high mean corpuscular volume and high red cell distribution width.

The mean and standard deviation value for anemia of chronic diseases concerning age is 47.17 and 9.538 which indicates that there is normal mean corpuscular volume and normal red cell distribution width.

DISCUSSION

'He who cures a disease may be the skill fullest, but he who prevents is the safest physician'

- Thomas Fuller

Anemia is a serious global health problem that affects individuals of all ages but particularly women of reproductive age. National Family Health Survey (NFHS -3) reveals the prevalence of anemia to be 70 -80% in children, 70% in pregnant women, and 24% in adult men.^[3] National Family Health Survey stated that 35 percent of women had mild anemia, 14.8 percent suffered from moderate anemia and 1.9 percent were affected severely. Besides iron deficiency, folic acid in pregnancy and vitamin B12 deficiencies in early childhood are also common prevalence of anemia in India is high because of low dietary intake, poor availability of iron, and chronic blood loss due to hookworm infestation and malaria.^[4] Causes of anemia include nutritional deficiencies, inherited genetic defects, medication-related side effects, and chronic disease. It can also occur because of blood loss from injury or internal bleeding, the destruction of red blood cells, or insufficient red blood cell production.^[5] The condition may be temporary or long-term and can manifest in mild or severe forms. The present study has been undertaken to diagnose and classify anemia based on Mean Corpuscular Volume and Red Cell Distribution Width from Bessman's study so that the patients are treated according to the cause without any unnecessary investigations and further treatment. Nutritional deficiency, alcoholism, and systemic diseases were also found to influence anemia.

New automated blood cell analyzers provide an index of red cell volume distribution width or heterogeneity and a histogram display of red cell volume distribution.^[6] Mean corpuscular volume and red cell distribution width are the two traditional principal criteria for the initial classification of anemic disorders. Evaluation of red cell distribution width and mean corpuscular volume to improve the classification of anemia from the blood count alone and to suggest the physiologic basis of a classification based on mean heterogeneity of red cell size.

The following discussion explains the relevance of various factors like age, sex, oral signs and symptoms, red blood cell count, hemoglobin%, mean corpuscular volume, mean corpuscular hemoglobin, hematocrit, Red Cell Distribution Width, ferritin, iron total iron binding capacity, vitamin b12, liver function tests and kidney function tests and its association with anemia.

Anemia is defined by the World Health Organization (WHO) as hemoglobin (Hb) levels <12.0 g/dL in women and <13.0 g/dL in men. Anemia is often multifactorial and is not an independent phenomenon. In one-third of the patients, anemia is due to nutritional deficiency, including iron, folate, or vitamin B12 deficiency; moreover, anemia of chronic disease accounts for about another third of the cases.^[7] Red blood cell distribution width (RDW) reflects erythrocyte size distribution, thus representing a reliable index of anisocytosis, widely used for the differential diagnosis of micro- and normocytic anemias.^[8] It has large use in diagnostic hematology. Red Blood Cell distribution width (RDW) is a simple measure of the broadness of erythrocyte size distribution, conventionally called anisocytosis. This measure is easily, inexpensively, and rapidly calculated as the ratio of standard deviation (SD) of red blood cell (RBC) volume and mean corpuscular volume (MCV) [i.e., $(RDW-SD)/(MCV) \times 100$], with the final result expressed as a percentage.^[9] No study explored the potential clinical usefulness of RDW for diagnosing anemia by correlating oral manifestations.

The present study shows male predilection in 10 males (33.30 %) and 20 females (66.70%), which was in accordance with the study conducted by **Anía BJ, Suman VJ, et al in 1997**, which stated that the incidence of anemia was higher among women

This is in accordance with **Anía BJ, Suman VJ et al in 1997**, who showed the incidence of anemia among older people is 4 to 6 times greater than that suspected clinically, and rises with age. The prevalence of anemia was higher among women in 65 years and men. The interpretation of these data is that women are more susceptible to anemia at a younger age due to menstrual blood loss and childbearing iron loss, while men have a higher prevalence of anemia-related morbidity at an older age.^[10]

Ohman SC et al 1986 evaluated the purpose of the prospective study to re-examine the relative importance of various factors in the pathogenesis of

angular cheilitis ^[11]. The results of this study indicated a correlation between angular cheilitis and pathogenic microorganisms. Furthermore, among dentate patients, a correlation exists between cutaneous discomfort and angular cheilitis. Other etiological factors suggested for this disorder were found to be of subordinate importance.^[12]

Graells J et al 2009, discussed the classic oral manifestations of vitamin B (12) deficiency and found that glossitis with linear lesions is an early clinical sign of vitamin B (12) deficiency and concluded the determination of vitamin B (12) in such patients, even in the absence of anemia.^[13]

In the present study, it has been found that as age advances hemoglobin percentage decreases in iron deficiency anemia, vitamin B12 as well as anemia of chronic diseases, which is in accordance with **Gerbrand J. Izaks et al in 1999**.^[14]

In the present study red cell distribution width is used as one of the main criteria for diagnosis of different types of anemia, which is in accordance with **Bessman JD et al in 1983** proposed improved classification of anemias by MCV and RDW values and reported that all patients with either iron, folate, or cobalamin deficiency had high RDW, as did those deficient in both iron and vitamin B12, even if both MCV and hemoglobin values were in the normal range. This has received attention for helping to distinguish between uncomplicated heterozygous thalassemia and iron deficiency.^[15] Red cell distribution width has also been shown to be a sensitive but nonspecific indicator of iron deficiency in long-term hemodialysis patients.

The oral cavity reflects the state of systemic health more frequently than any other part of the body. Anemia occurs as a result of a combination of many predisposing factors. The present study reflects the sensitivity of oral mucosa to iron deficiency, nutritional deficiency, and anemia of chronic diseases and classifies anemia based on mean corpuscular volume and red cell distribution width.

The hematological screening includes estimations of red blood count, hemoglobin%, mean corpuscular volume, mean corpuscular hemoglobin, hematocrit, red cell distribution width, ferritin, iron, total iron binding capacity, vitamin B12, liver function tests, and kidney function tests.

Anemia can be classified by the appearance of red blood count on the peripheral blood smear by its

size i.e., microcytic, normocytic, or macrocytic, or by the concentration of hemoglobin i.e.,

hypochromic, normochromic. Hemoglobin is the initial marker for diagnosing anemia.

Hemoglobin%	>10	<10
Iron deficiency anemia	66.67%	33.33%
Vitamin B12 deficiency	75%	25%
Anemia of chronic diseases	-	100%

Measuring hemoglobin levels should be included in a routine physical examination to establish the normal value. Because of the narrow intra-

individual variation of hemoglobin, even minor deviations from this value may be the first sign of more severe disease.

RDW	MCV<80fl (microcytosis)	MCV=80~100fl (normocytic)	MCV>100fl (macrocytosis)
Low	ACD	ACD	Normal
High	IDA	Early iron or VitaminB12	Vitamin B12

Nutritional deficiency, whether of iron or vitamin B12 always cause an increased red cell volume heterogeneity. While these patients are anemic on average, even those who are not anemic have high red cell distribution width. As the nutritional deficiency has more abnormal cells and admixed in the peripheral blood. In early or mixed nutritional deficiency, red cell distribution width is high, while the mean corpuscular volume remains within the normal range; heterogeneous normocytic indices thus are the first clue.

Anemia of chronic diseases is the most common type of anemia among hospitalized patients, and it can coexist with other common anemias.^[16] The red cell distribution width in the patients with anemia of chronic diseases has been found normal possibly reflecting that it is not well classified by either mean corpuscular volume and red cell distribution width.

LIMITATION :

The present study reflects the sensitivity of oral mucosa to iron deficiency, nutritional deficiency, and anemia of chronic diseases and classifies anemia based on mean corpuscular volume and red cell distribution width. There have been a variety of etiological factors quoted for anemia like nutritional deficiencies, inherited genetic defects, medication-related side effects, chronic disease, Vit B12, iron, and autoimmunity. It can also occur because of blood loss from injury or internal bleeding, the destruction of red blood cells, or insufficient red blood cell production. Further comparative studies with a larger sample size and various types of anemia with various etiological factors would be required with clear distinction.

CONCLUSION:

The occurrence of anemia has significantly

increased during the past few years. There have been a variety of etiological factors quoted for anemia like nutritional deficiencies, inherited genetic defects, medication-related side effects, chronic disease, Vit B12, iron, and autoimmunity. It can also occur because of blood loss from injury or internal bleeding, the destruction of red blood cells, or insufficient red blood cell production.

The oral cavity reflects the state of systemic health more frequently than any other part of the body. Anemia occurs as a result of a combination of many predisposing factors. Mean Corpuscular Volume and Red Cell Distribution Width are the two traditional principal criteria for the initial classification of anemic disorders. Improved classification of anemia from the traditional blood count alone was proposed based on the physiologic parameters.

The study was done to determine the type of anemia by evaluating the oral changes based on the classification of anemia by Mean Corpuscular Volume and Red Cell Volume Distribution Width, Red blood cells from initial blood count can provide a rapid and useful guide in our daily practice. It is easy to practice and many unnecessary medical examinations can be saved.

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