DHA TELEHEALTH CLINICAL

GUIDELINES FOR VIRTUAL

MANAGEMENT OF ANEMIA - 37

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INTRODUCTION

Dubai Health Authority (DHA) is the responsible entity for regulating, licensing and monitoring health facilities and healthcare professionals in the Emirate of Dubai. The Health Regulation Sector (HRS) is an integral part of DHA and was founded to fulfil the following overarching strategic objectives:

Objective #1: Regulate the Health Sector and assure appropriate controls are in place for safe, effective and high-quality care.

Objective #2: Position Dubai as a global medical destination by introducing a value-based, comprehensive, integrated and high-quality service delivery system.

Objective #3: Direct resources to ensure happy, healthy and safe environment for Dubai population.

ACKNOWLEDGMENT

This document was developed for the Virtual Management of Anemia in collaboration with Subject Matter Experts. The Health Policy and Standards Department would like to acknowledge and thank these professionals for their dedication toward improving the quality and safety of healthcare services.

The Health Regulation Sector

Dubai Health Authority

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EXECUTIVE SUMMARY

Telehealth is based on Evidence Based Practice (EBP) which is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence and guidelines from systematic research.

EBP is important because it aims to provide the most effective care virtually, with the aim of improving patient outcomes. As health professionals, part of providing a professional service is ensuring that practice is informed by the best available evidence.

This guideline is presented in the format comprising of clinical history/symptoms, differential diagnosis, investigations and management. Identification of 'Red Flags' or serious conditions associated with the disease is an essential part of this telehealth guideline as it aids the physician to manage patients safely and appropriately by referrals to ER, family physicians or specialists for a face to face management.

DEFINITIONS/ABBREVIATIONS

Virtual Clinical Assessment: Is the evaluation of the patient's medical condition virtually via telephone or video call consultations, which may include one or more of the following: patient medical history, physical examination and diagnostic investigations.

Patient: The person who receives the healthcare services or the medical investigation or treatment provided by a DHA licensed healthcare professional.

ABBREVIATIONS

BUN	:	Blood Urea Nitrogen
CBC	:	Complete Blood Count
CT	:	Computed Tomography
DHA	:	Dubai Health Authority
DIC	:	Disseminated Intravascular Coagulation
EBP	:	Evidence Based Practice
ER	:	Emergency Room
FBC	:	Full Blood Count
GI	:	Gastrointestinal
HPLC	:	Hemoglobin Electrophoresis or Liquid Chromatography
HRS	:	Health Regulation Sector
MCV	:	Mean Corpuscular Volume

RBC	:	Red Blood Cell
RDW	:	Red Cell Width
TIBC	:	Total Iron Binding Capacity
TTP	:	Thrombocytopenic Purpura

1. BACKGROUND

1.1. Anemia is defined as a hemoglobin (Hb) level <12 g/dL in females and <14 g/dL in males or, alternatively, as an Hb level <12.5 g/dL in adults. Risk factors include extremes of age, female gender, lactation, and pregnancy. The most common cause internationally is iron deficiency.

1.2. Anemia can cause significant morbidity if left untreated and is often the presenting sign of a more serious underlying condition. The rate at which anemia develops is often as important as the severity, as a rapid decline can overwhelm the compensatory mechanisms of the body.

1.3. Causes

1.3.1. The three most common causes in clinical practice are iron deficiency, alpha or beta thalassemia minor, and (less often) the anemia of inflammation (anemia of chronic disease). Since all may have hypochromic and microcytic RBCs, other tests must be used to establish the diagnosis.

a. Iron deficiency anemia – Important discriminating features are a low serum ferritin concentration, an increased total iron binding capacity (transferrin), and low serum iron concentration, resulting in a low transferrin saturation. For clinicians making this diagnosis, it is

mandatory to determine the cause of the iron deficient state (eg, occult colonic carcinoma, excessive menstrual losses).

b. Alpha or beta thalassemia minor – Adults with thalassemia are most often heterozygotes for the alpha or beta forms of this syndrome and may be only minimally anemic. A family history is therefore often negative. The peripheral smear shows varying degrees of hypochromia, microcytosis, target cells, tear-drop forms, and basophilic stippling. The RBC count may be increased; uncomplicated patients have normal or increased iron stores. The diagnosis of beta thalassemia trait can often be made by demonstrating increased levels of hemoglobin A_2 on hemoglobin electrophoresis or liquid chromatography (HPLC), while molecular methods are usually required for the diagnosis of the alpha thalassemia variants.

c. Anemia of inflammation – The hallmarks of this condition include a low serum iron, low total iron binding capacity (transferrin), and a normal to increased serum ferritin concentration. Although hypochromic and microcytic red cells can be found in these patients, a low MCV is most frequently seen only in those patients with hepatoma or renal cell carcinoma.

1.4. Etiology

1.4.1. Genetic etiologies include the following:

a. Hemoglobinopathies

b. Thalassemias

c. Enzyme abnormalities of the glycolytic pathways

d. Defects of the RBC cytoskeleton

e. Congenital dyserythropoietic anemia

f. Rh null disease

g. Hereditary xerocytosis

h. Abetalipoproteinemia

i. Fanconi anemia

1.4.2. Nutritional etiologies include the following:

a. Iron deficiency

b. Vitamin B-12 deficiency

c. Folate deficiency

d. Starvation and generalized malnutrition

1.4.3. Physical etiologies include the following:

a. Trauma

b. Burns

c. Frostbite

d. Prosthetic valves and surfaces

1.4.4. Chronic disease and malignant etiologies include the following:

a. Renal disease

b. Hepatic disease

c. Chronic infections

d. Neoplasia

e. Collagen vascular diseases

1.4.5. Infectious etiologies include the following:

a. Viral - Hepatitis, infectious mononucleosis, cytomegalovirus

b. Bacterial - Clostridia, gram-negative sepsis

c. Protozoal - Malaria, leishmaniasis, toxoplasmosis

2. SCOPE

2.1. Telehealth services in DHA licensed Health Facilities.

3. PURPOSE

3.1. To support the implementation of Telehealth services for patients with complaints of Anemia in Dubai Health Authority (DHA) licensed Health Facilities

4. APPLICABILITY

4.1. DHA licensed physicians and health facilities providing Telehealth services.

4.2. Exclusion for Telehealth services are as follows

4.2.1. Emergency cases where immediate intervention or referral is required

4.2.2. Prescribe Narcotics, Controlled or Semi-Controlled medications`

5. CLINICAL SYMPTOMS

5.1. Typical symptoms include:

5.1.1. Fatigue

5.1.2. Weakness

5.1.3. Headache

5.1.4. Irritability

5.1.5. Exercise intolerance

5.1.6. Exertional dyspnea

5.1.7. Vertigo

5.1.8. Angina pectoris

5.2. Initial approach — Anemia is one of the major signs of disease. The history and simple laboratory testing are useful in evaluating the anemic patient.

5.3. History — There are several important components to the history in the setting of anemia:

5.3.1. Is there a recent history of loss of appetite, weight loss, fever, and/or night sweats that might indicate the presence of infection or malignancy?

5.3.2. Is there a history of, or symptoms related to, a medical condition that is known to result in anemia (eg, tarry stools in a patient with ulcer-type pain, significant blood loss from other sites, rheumatoid arthritis, renal failure)?

5.3.3. Is the anemia of recent origin, subacute, or lifelong? Recent anemia is almost always an acquired disorder, while lifelong anemia, particularly if accompanied by a positive family history, is likely to be inherited (e.g. the hemoglobinopathies, thalassemia, hereditary spherocytosis).

5.3.4. Abnormal urine color can occur in renal and hepatic disease and in hemolytic anemia.

5.3.5. A thorough dietary history is important in a patient who is anemic. This history must include foods that the patient eats and those that he/she avoids, as well as an estimate of their quantity. A meal-by-meal description is necessary to obtain appropriate estimates.

5.3.6. Nutritional deficiencies may be associated with unusual symptoms that can be elicited by a history. Patients with iron deficiencies frequently

chew or suck ice (pagophagia). Occasionally, they complain of dysphagia, brittle fingernails, relative impotence, fatigue, and cramps in the calves on climbing stairs that are out of proportion to their anemia.

5.3.7. In vitamin B-12 deficiency, early graying of the hair, a burning sensation in the tongue, and a loss of proprioception are common. Suspect a loss of proprioception if the patient stumbles in the dark or must look in order to put on pants in the morning. Paresthesia or unusual sensations frequently described as pain also occur in pernicious anemia

5.3.8. Patients with folate deficiency may have a sore tongue, cheilosis, and symptoms associated with steatorrhea. Color, bulk, frequency, and odor of stools and whether the feces float or sink can be helpful in detecting malabsorption. More sensitive questions to detect steatorrhea include whether the toilet needs to be flushed more than once to rid it of stool and whether an oily substance is floating on the water surface after the first flush

5.3.9. Obtain a history of fever or identify the presence of fever, because infections, neoplasms, and collagen vascular disease can cause anemia. Similarly, the occurrence of purpura, ecchymoses, and petechiae suggest the occurrence of either thrombocytopenia or other bleeding disorders.

5.3.10. Cold intolerance can be an important symptom of hypothyroidism or lupus erythematosus, paroxysmal cold hemoglobinuria, and certain macroglobulinemias

5.3.11. The patient's ethnicity and country of origin may be helpful, as the thalassemias and other hemoglobinopathies are particularly common in patients from the Mediterranean, Middle East, Sub-Saharan Africa, and Southeast Asia.

5.3.12. The use of medications, both prescribed and over-the-counter - Specific questions should be asked about the use of alcohol, aspirin, and nonsteroidal anti-inflammatory drugs.

5.3.13. A past history of blood transfusions, liver disease, treatment of the patient (or other family members) with iron or other hematinics, herbal preparations, and exposure to toxic chemicals in the workplace or environment should also be obtained. An assessment of nutritional status is especially important in older adults and alcoholics.

5.3.14. If there is a history of recent surgery, ongoing blood loss at the surgical site must be considered. A detailed history of the pre-, intra-, and postoperative course should be obtained, including any complications noted during the operation. A history of bleeding disorders or excessive

bruising may indicate an underlying coagulation disorder. Any antibiotics administered should be noted, as some can produce a decrease in platelet levels.

6. RED FLAGS/LIFE-THREATENING CONDITIONS

6.1. Red flags

6.1.1. Tachycardia, signs of cardiac failure

6.1.2. Features of haemolysis (dark urine, jaundice, scleral icterus)

6.1.3. Associated reticulocytopenia or reticulocytosis

6.1.4. Presence of nucleated red blood cells on blood film

6.1.5. Associated thrombocytopenia or neutropenia may indicate malignancy or an infiltrative disorder

6.1.6. Severe vitamin B12 or folate deficiency

6.1.7. Severe symptomatic anemia

6.2. Life Threatening conditions

6.2.1. Acute haemorrhage

Causes of acute hemorrhage include trauma (such as major fractures, crush injuries), acute gastrointestinal (GI) bleeding, rupture of a vascular aneurysm (especially abdominal aortic aneurysm), and recent surgery.

6.2.2. Microangiopathic hemolytic anemias

Hemolytic uremic syndrome, disseminated intravascular coagulation (DIC), and thrombotic thrombocytopenic purpura (TTP) produce life-threatening rapid hemolysis.

6.2.3. Sickle cell vaso-occlusive crisis

This is a common complication of sickle cell anemia, which presents with severe pain precipitated by cold, dehydration, infection, or ischemia (often due to strenuous exercise). The crisis may give rise to skeletal pain due to bone infarction or avascular necrosis, especially of the hip or shoulder. Other presentations include acute abdominal pain and acute chest syndrome, which is clinically indistinguishable from pneumonia.

6.2.4. Leukemias or aplastic anemia

Usually present with a normocytic anemia and coexisting neutropenia and thrombocytopenia. Circulating blasts may be reported on peripheral smear. If these conditions are suspected, an immediate hematology consultation is required for bone marrow biopsy

6.2.5. Decreased physiologic reserve

It is important to identify patients with decreased physiologic reserve, such as those with coexisting cardiovascular or pulmonary disease, as

these patients are less able to tolerate anemia and have more severe symptoms.

7. DIFFERENTIAL DIAGNOSIS

Refer to APPENDIX 1 for algorithm for the assessment of anemia

7.1. Microcytic anemia (MCV < 80)

7.1.1. Iron Deficiency Anemia

7.1.2. Anemia of chronic conditions

7.1.3. Haemoglobinopathies, e.g. thalassemia

7.1.4. Sideroblastic anemias

7.1.5. Refer to APPENDIX 2 for Summary of Microcytic Anemia

7.2. Normocytic anemia (MCV 80 -100)

7.2.1. Aplastic Anemia

7.2.2. Hemolytic Anemia

7.2.3. Hemorrhage

7.2.4. Leukemia

7.2.5. Other bone marrow

7.3. Macrocytic anemia (MCV > 100)

7.3.1. Vitamin B 12 deficiency

7.3.2. Folate deficiency

7.3.3. Drug induced

7.3.4. Alcohol abuse

7.3.5. Myelodysplastic syndrome

7.3.6. Liver diseases

8. INVESTIGATION

8.1. Tests are guided by the history and the suspected etiology of active bleeding. These may include the following procedures.

8.1.1. The first step in diagnosis is to identify the type of anemia that is present, using the results of the CBC. Due to their relative reproducibility, mean corpuscular volume (MCV) and red cell width (RDW) are the most useful components in the initial classification of most anemias.

8.1.2. A serum ferritin, serum iron levels and total iron binding capacity (TIBC).

8.1.3. Consider testing for Vitamin B12 and folate level

8.1.4. Prothrombin time/activated partial prothrombin time, which is usually normal, but tested to identify patients with decreased coagulation due to anticoagulants, underlying defects in hemostasis, or consumptive coagulopathy.

8.1.5. In patients with upper GI bleeding, elevated BUN may be seen, even in absence of renal issues, due to digestion of blood, which is a source of urea.

8.1.6. Abdominal ultrasound scan: allows rapid identification of intra-abdominal bleeding and indicated if abdominal trauma or a ruptured abdominal aortic aneurysm are suspected.

8.1.7. Joint x-rays, indicated in patients with trauma to identify fractures. Long-bone fractures can be a significant source of bleeding.

8.1.8. Upper GI endoscopy, required to identify sources of upper GI bleeding.

8.1.9. Colonoscopy, required to identify sources of lower GI bleeding. A retrospective review of the medical records of a sample of patients with colorectal cancer found that anemia was one of the commonest symptoms/signs in those considered to have had a missed diagnostic opportunity

8.1.10. Capsule endoscopy may have diagnostic, but not therapeutic, utility in situations where there is concern for GI bleeding in inaccessible areas such as the small bowel.

8.1.11. Exploratory laparotomy, which may be required in patients with abdominal bleeding to identify the source, especially if there is a history of abdominal trauma or previous abdominal surgery.

8.1.12. Computed tomography (CT) scanning of the body region affected by trauma or aneurysm rupture, which will identify internal injuries or the extent and nature of the aneurysm, and identify sources of bleeding.

8.2. Many anemic patients with no acute or active bleeding are asymptomatic, and the anemia is only noted on a CBC taken as part of the assessment of an unrelated condition.

9. REFERRAL CRITERIA

9.1. Referral Criteria to Family Physician/Specialist

9.1.1. Unexplained progressive symptomatic anemia

9.1.2. Anemia in association with other cytopenia

9.1.3. Persistent unexplained anemia

9.1.4. Iron deficiency anemia showing sub-optimal response to oral iron therapy

9.1.5. B12 deficiency of uncertain cause requiring further investigation

9.1.6. Associated reticulocytopenia or reticulocytosis

9.1.7. Presence of nucleated red blood cells on blood film

9.1.8. Severe vitamin B12 or folate deficiency

9.1.9. Severe symptomatic anemia

9.2. Referral Criteria to Emergency Department:

9.2.1. Suspected Aplastic anemia

9.2.2. Tachycardia, signs of cardiac failure

9.2.3. Features of haemolysis (dark urine, jaundice, scleral icterus)

9.2.4. Associated thrombocytopenia or neutropenia may indicate malignancy or an infiltrative disorder

9.2.5. Sickle cell vaso-occlusive crisis

9.2.6. Acute hemorrhage

10. MANAGEMENT AND TREATMENT

10.1. Refer to APPENDIX 3 for the Virtual Management of Anemia Algorithm

10.2. The purpose of establishing the etiology of an anemia is to permit selection of a specific and effective therapy.

10.3. Therapeutic approaches to anemia include the use of blood and blood products, immunotherapies, hormonal/nutritional therapies, and adjunctive therapies. The goal of therapy in acute anemia is to restore the hemodynamics of the vascular systems and to replace lost red blood cells. To achieve this, the practitioner may use

mineral and vitamin supplements, blood transfusions, vasopressors, and glucocorticosteroids.

10.4. Treatment of iron deficiency anemia in adults

10.4.1. The first-line management of iron deficiency anemia is to prevent further blood loss by treating the underlying cause. Treatments that reduce menstrual loss should be considered in premenopausal women, e.g. hormonal contraceptives (including Mirena) or tranexamic acid. Consider stopping or reducing the dose of any medicine that may be contributing to blood loss.

10.4.2. Review and correct any dietary factors that may be contributing to the anemia, e.g. low dietary iron intake in people adhering to a vegan diet. Dietary iron is available in two forms:

a. Heme iron: found in animal muscle and blood. This form is absorbed independent of other dietary factors. Iron found in meat, fish and poultry are bioavailable.

b. Nonheme iron: found in animal products and plant foods. This form is absorbed depending on dietary factors. Iron found in plant sources are less well absorbed. However, including enhancers such as ascorbic acid or vitamin C improves iron absorption from these foods. Fruits

and vegetables contain vitamin C and organic acids thus aid the absorption of nonheme iron.

10.4.3. Dietary advice will include:

a. Adding heme iron from animal-source foods to foods containing non-heme iron increase the overall bioavailability and absorption of iron from a meal.

b. Dairy products and eggs are very poor sources of iron and decrease iron absorption: iron absorption is inhibited due to caseins from milk and certain forms of calcium.

c. Tea, coffee, and cocoa are known as inhibitors: should not be consumed with meals as they inhibit the absorption of nonheme iron.

d. Alcohol intake enhances iron absorption; however, it is not recommended to use alcohol for regulating iron status. but should not be used as a means of regulating iron status. Alcohol consumption is associated with a 40% reduction in the risk of iron deficiency anemia

10.4.4. Vitamin A and carotenoids enhance iron absorption by overcoming the inhibiting effect of polyphenols and phytates (found in whole grains) on iron absorption. Vitamin A is found in:

a. Plant-source foods (e.g. green leafy vegetables, orange/ yellow fruits and vegetables) in the form of pro-carotenoids.

b. Dairy products, eggs, fish oil and liver in the form of retinol.

10.4.5. Patients diagnosed with coeliac disease should begin a gluten free diet. Correction of depleted iron and other nutritional deficiencies with supplementary iron, vitamin B12, folate, calcium and vitamin D is often necessary.

10.4.6. Oral iron supplementation, 100 – 200 mg elemental iron per day. A fully subsidized option is ferrous fumarate, 200 mg tablets (65 mg elemental iron), which would require a dose of two to three tablets daily for an adult with iron deficiency anemia. If ferrous fumarate is not tolerated, consider oral ferrous sulphate 325 mg tablets (105 mg elemental iron), one to two tablets daily; this is partially subsidized. A 325 mg ferrous sulphate tablet formulated with 350 mg folic acid is also available, partially subsidized.

10.4.7. A failure to respond to treatment may indicate ongoing iron loss and these patients will generally require gastrointestinal investigation.

10.4.8. Refer to APPENDIX 4 for Summary of Iron Supplementation.

10.4.9. For optimal iron absorption, supplements should be taken on an empty stomach. Gastrointestinal irritation can occur with oral iron, including

nausea, epigastric pain and altered bowel function (constipation or diarrhea). Patients should be advised to continue with their iron supplementation if symptoms arise, but to discuss these symptoms with their General Practitioner. If gastric symptoms occur, advise the patient to try taking the supplement with food. Increasing fiber and fluid intake can also be helpful for constipation. Alternate day dosing may be appropriate for some patients to reduce adverse effects.

10.4.10. In patients receiving oral iron supplementation, the hemoglobin concentration should rise by approximately 0.1 g/dL, per day, and should be approximately 2 g/dL higher after three to four weeks, Hemoglobin levels (FBC) should be checked periodically to assess response to treatment, particularly in the early stages if the patient has significant anemia. Once levels return to normal, treatment should be continued for a further three months to replenish iron stores. Ferritin levels should be checked four to six weeks after completing treatment to confirm that iron stores have been replaced.

10.4.11. Iron transfusion may be considered for patients who are unable to tolerate oral iron supplementation and patients with malabsorption that prevents the uptake of oral iron.

10.4.12. Blood transfusions for patients with iron deficiency anemia are generally only required where there is a risk of cardiovascular instability due to severe anemia, or if patients have symptomatic anemia despite iron treatment. The goal of a transfusion is to restore hemoglobin to a safe, but not necessarily normal, level.

10.4.13. For patients with vitamin B12 deficiency or folate deficiency, Vitamin B12 is only found in animal-source foods such as shellfish, beef liver, other meats, fish and poultry, and dairy products. Folate is naturally found in legumes and green leafy vegetables, whole grains and fruits and fruit juices such as oranges.

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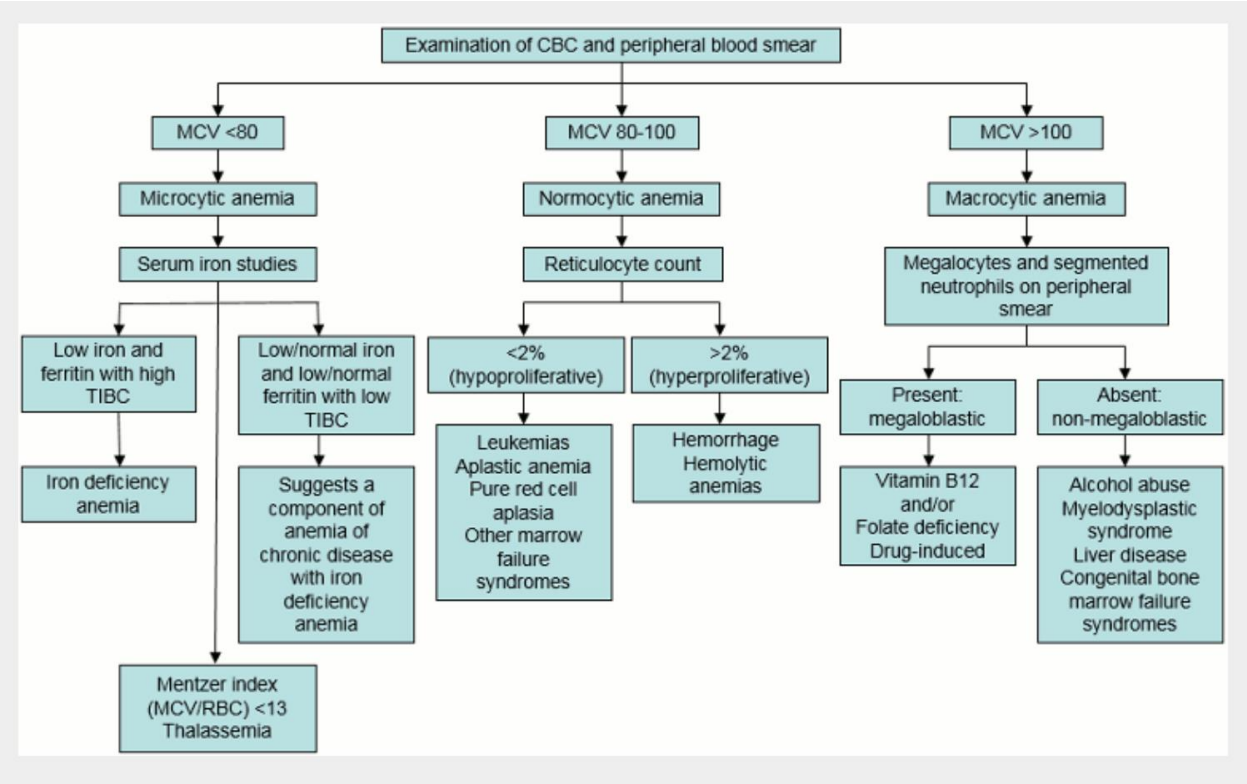
APPENDICES

APPENDIX 1 – ALGORITHM FOR THE ASSESSMENT OF ANEMIA



APPENDIX 2 – SUMMARY OF MICROCYTIC ANEMIA

Test	Microcytic Anemia Due to			
	Iron Deficiency	Thalassemia	Chronic Inflammation	Sideroblastic Anemia
FEP level	High	Normal	Normal	Normal
Ferritin level	Low	Normal to increased	High	Normal to increased
MCV	Low	Low	Low or normal	Low, normal, or high
Percentage saturation	Low	Increased	Normal	Normal
RDW	High	Normal to high	Normal	High
Serum iron level	Low	Normal	Low	Normal
Serum TfR level	High	Normal	Normal	Normal
TIBC level	High	Normal	Low	Normal

FEP represents free erythrocyte protoporphyrin; MCV, mean corpuscular volume; RDW, red cell distribution width; TfR, serum transferrin receptor; TIBC, total iron binding capacity.
*The microcytic anemias are presented in decreasing order of prevalence.

APPENDIX 3 – IRON SUPPLEMENTATION

Iron salt	Dose	Elemental iron content
Ferrous fumarate	200 mg	65 mg
Ferrous sulfate (tablet)	325 mg	105 mg
Ferrous sulfate (liquid)	150 mg (in 5 mL)	30 mg (in 5 mL)

APPENDIX 4 – VIRTUAL MANAGEMENT OF ANEMIA ALGORITHM