PRELIMINARY STUDIES OF
ANEMIA IN OUTPATIENTS

Thesis Submitted In Partial Fulfilment For
The Master Degree In General Medicine

BY

AMR HASSAN HEMIDA

M.B., B.Ch.

Supervised By

Prof. Dr. MOHAMED SADEK SABOUR
Professor Of General Medicine
Ain Shams University

Dr. SALWA MOHAMED YOUSSEF
Lecturer Of Clinical Pathology
Ain Shams University

AIN SHAMS UNIVERSITY

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A C K N O W L E D G E M E N T

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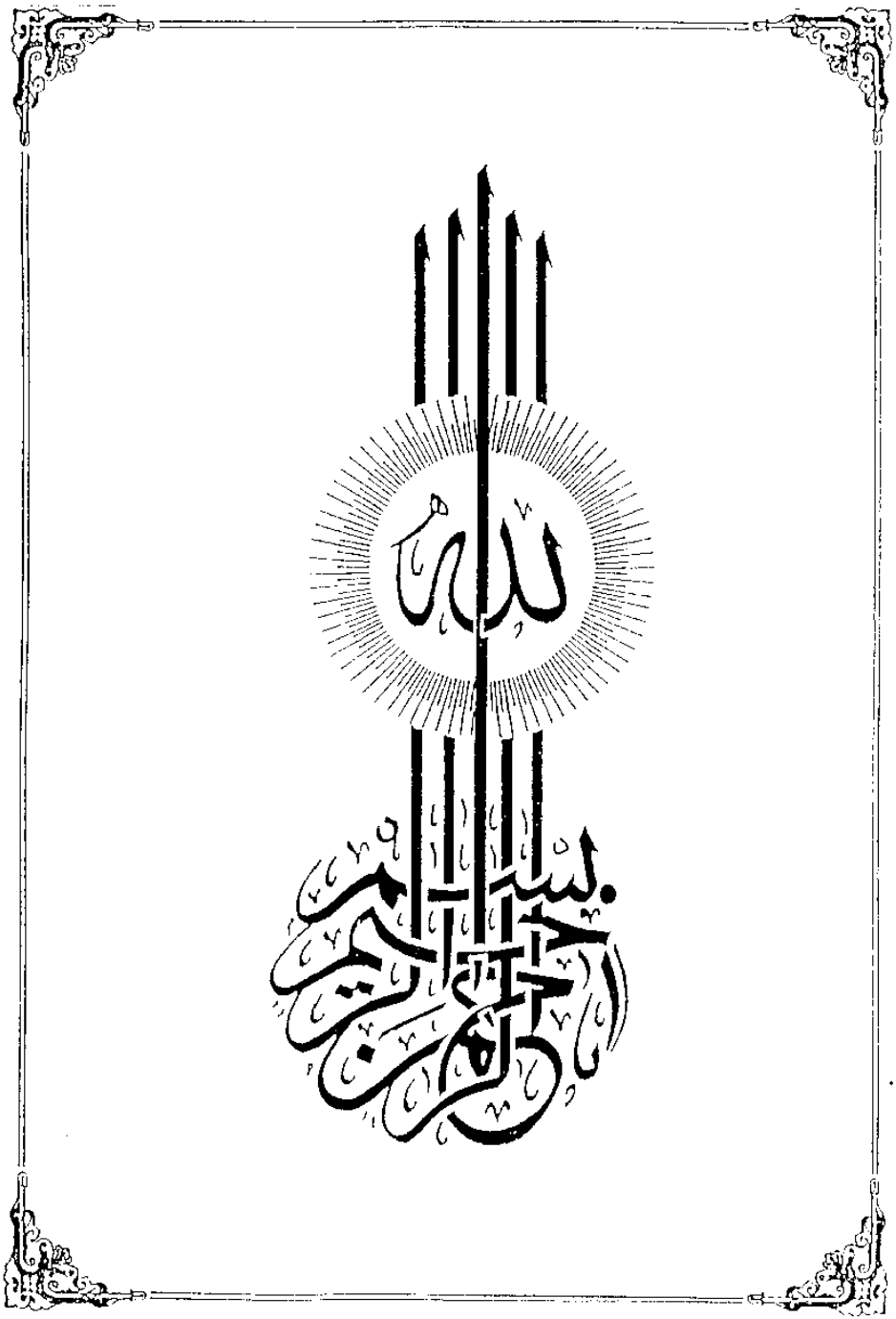

C O N T E N T S

INTRODUCTION
and
AIM OF THE WORK

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Anemia is a prevalent ailment in Egypt. Red cell count, MCV, MCH and MCHC are sufficient screening procedures for most clinical purposes.

An accurate diagnosis is simply achieved by blood film examination, reticulocytic count and quantitative cell count. In other cases bone marvow aspiration or further studies might be required.

The choice of tests to be undrtaken depend upon the result of the preliminary tests.

The aim of the present work is the classification and investigation of anemia detected among different patients attending various outpatient clinics at Ain Shams University hospitals in attempt to throw a light on the prevalent types of anemia.

REVIEW OF LITERATURE

If the anemia has been insidious in onset and cardiopulmonary disease is absent, the patient's adjustment may be so good that the hematocrit may be 0.25 the normal value or less and the hemoglobin concentration 8 gm/dl or lower, before the patient experiences sufficient symptoms (Dawson et al., 1969) to appreciate his true situation. It is common for patients with iron-deficiency anemia, pernicious anemia or other types of slowly developing anemia to have their hemoglobin concentrations fall to 6 gm/dl before they are motivated to seek medical attention (Desforges, 1970).

In children, particularly, there may be little apparent restriction of capacity for physical exertion despite the presence of severe anemia (Cropp, 1969). The physiologic adjustments that take place chiefly involve the cardiovascular system and changes in the hemoglobin oxygen dissociation curve. The symptoms of acute hemorrhage are chiefly related to hypovolemia, rather than to anemia. Depending on the amount of blood lost, there may be no symptoms, mild hypotension, or progressively severe degree of shock (Weil, shubin, 1967).

When there is acute hemolytic reaction, Jaundice may develop without bile in the urine (acholuric Jaundice). If intravascular hemolysis occurs, there may be hemoglobinuria, methemoglobinemia and hemoglobinuria, as well as fever and abdominal or back pain These manifestations are related to sudden release of hemoglobin, and to its destruction and disposal. They occur in addition to cardiorespiratory symptoms that result from the anemia per se (Ham., 1955).

- In chronic anemia, the reduction in the concentration of oxygen-carrying pigment in the blood has a meaningful correlation with cardiovascular adjustments that must be made than does the magnitude of the deficit in the total quantity of red blood cells or of hemoglobin in the circulation (Korner, 1959).

The amount of oxygen delivered to the tissues by a given volume of blood is a function of (1) the concentration of hemoglobin, (2) the percent saturation of hemoglobin with oxygen, (3) the hemoglobin-oxygen dissociation curve, and (4) the tissue oxgyen tension. When fully saturated with oxygen, 1 gm of hemoglobin will bind 1.34 ml of oxygen. At a normal

This is helpful, but a reduction in the arterial oxygen saturation (Rankin et al., 1961) also occurs and this is disadvantageous. The demand for a greater cardiac output is first accomplished by an accelerated heart rate, rather than by a change in stroke volume (Brannon et al., 1945). Hence, tachycardia at rest and especially upon small exertion is characteristic of the patient with the greater degrees of anemia (Elbert et al., 1941).

* The binding and release of oxygen by hemoglobin are profoundly affected by the variations in the concentration of phosphates, especially 2,3-diphosphoglyceric acid (2,3-DPG) (Astrup, 1970).
The oxygen affinity of hemoglobin is reduced as the concentration of 2,3 DPG increases and the converse is also true (Harkness, 1970). An increase in red cell 2,3 DPG is found in chronic anemia (Benesch and Benesch, 1969). This facilitates the delivary of oxygen to the tissues by reducing the affinity of hemoglobin for oxygen at oxygen tensions found in capillaries (Torrance et al., 1970). At alveolar oxygen tensions, the small change in oxygen affinity that is due to the increased red cell 2,3 DPG does not significantly affect the uptake of

oxygen by the red cells in the lungs. The net result favors the heart by allowing the tissues to extract oxygen during exercise at a lower cardiac index for an equivalent oxygen consumption and work load than otherwise would be the case (Oski et al., 1971). It has been calculated that DPG-induced changes in hemoglobin affinity for oxygen may compensate for up to half the expected oxygen deficit in anemia (Oski et al., 1971).

* Cardiovascular adjustments :-

The cardiac index generally is increased in anemia, and the arteriovenous oxygen difference is narrowed (Brannon, et al., 1945). Central venous and intracardiac pressures are not altered, although at times the right atrial pressures may be elevated. The total circulating blood volume may decrease (Blumgart and Altschule, 1948), although this does not occur uniformly (Sproule et al., 1960). When the hemoglobin concentration is less than 7 gm/dl , the cardiac output is nearly always increased(Brannon et al., 1945) and when it is less than 5 gm/dl, the increase in cardiac index has been found to be due mainly to an increase in the stroke volume and to a lesser extent, in heart rate, (Roy et al., 1963)

especially with exercise. By contrast, in persons without anemia the increase in cardiac output accompanying exercise is mainly due to tachycardia. In children with severe anemia, the mean cardiac index has has been found to be approximately the same as adults with equally severe anemia. However, in children this states was achieved by greater tachycardia and a lesser increase in stroke volume than in comparably anemic adults (Cropp, 1969). Nevertheless , the capacity of children with anemia to endure exercise burdens generally is excellant (Parsons and Wright, 1939). If congestive heart failure develops, there is usually some underlying heart disease. However, the latter may not be the case in adults if the hemoglobin cancentration is less than 5 gm/dl (Bartels, 1937).

Cardiac compensation may be marginal in severe anemia and congestive heart failure may be precipitated by blood transfusion (Graettinger et al., 1963) unless precautions are taken (Duke et al., 1954). As the cardiovasculor system adapts to anemia generally the velocity of blood flow is increased (Duke and Abelman, 1969) and hence the circulation

time is shortened; this condition may persist even with the development of congestive heart failure (Friedberg, 1969). Studies have shown that mild or moderate anemia is accompanied by a greater coronary flow per unit of left ventricular work ; ultimately, however, when the hemoglobin concentration is reduced below half of normal, impaired ventricular function is observed, presumbly because of the coronary flow has approached maximum (Case et al., 1955). Whereas reflex vasoconstriction is a feature of the response to acute blood loss (Ebert et al., 1941), in chronic anemia the peripheral vascular resistance is lowered and this plays a dominent role in the high output hyperkinetic circulatory response (Duke and Abelman, 1969). Increasing peripheral resistance as with methoxamine or orthostatic stress reduce cardiac output (Duke and Abelman, 1969).
Changes in peripheral resistance are regional,rather than generalised. Muscle blood flow is increased, whereas skin blood flow is reduced (Abramson et al., 1943). Cerebral blood flow is increased (Heyman et al., 1952) and renal blood flow is diminished (Bradley and Bradley, 1947). Usually the systemic and pulmonary artery systolic pressures are unaffected, but the diastolic pressures are lower (Roy et al., 1963).

* Respiratory and circulatory symptoms :-

Respiratory and circulatory symptoms are only noticeable following exertion or excitement; however, when the anemia is sufficiently severe, dyspnea and awareness of vigourous or rapid heart action may be noted even at rest. A humming or whirring sound in the head, which is attributed to the rapid blood flow through cranial arteries, may be bothersome to the patient and signal the point at which significant anemia has developed. The rapidity of the onset of anemia, its severity, the age of the patient and the capacity of cardiovascular system to adjust to it govern the clinical presentation. When anemia develops rapidly, shortness of breath, tachycardia, pallor, "dizziness" or faintness, particularly upon arising from a sitting or recumbent posture and extreme fatigue are prominent. In chronic anemia, only moderate dyspnea or palpitation may occur, but patients have been observed in whom the clinical picture of congestive heart failure (Bartels, 1973), angina pectoris, or intermittent claudication (Pickering and Wayne, 1933), was the presenting manifestation. Salt and water retention in anemia (Whitaker, 1956) may result when blood flow to the kidney is diminished (Bradley and Bradley, 1947).

The mechanical properties of the lungs were normal in a series of patients with anemia (Mcllory et al., 1956). However, along with the cardiovoscular symptoms, the rate and depth of respiration often are increased. The minute ventilation is increased, as is the residual air (Rankin et al., 1961), but the forced expiratory volume is reduced (Blumgart and Altschul, 1948). At rest the arterial oxygen tension was found to be lower in anemic patients than in normal subjects (Ryan and Hickam, 1952) and as consequence the alveolar blood oxygen tension gradient was higher than normal. During strenuous exercise, a marked depression of both oxygen uptake and CO_2 production was found in anemic individuals when compared with normal persons exercising at comparable level (Sproule et al., 1960). The additional oxygen cost of work in the anemic state and cardiopulmonary adjustments to physical exertion have been carefully studied in persons with iron deficiency anemia (Andersen and Barkve, 1970). The oxygen debt incurred during a standard work load and rate of work was greater in the anemic subject than in the same person after recovery from anemia. In the anemic state, it took longer to restore heart rate and respiratory minute volume to pre-exercise