SUSCEPTIBILITY TO INFECTION IN HAEMOLYTIC ANAEMIA

Essay
Submitted for Partial Fulfilment of
Master Degree (M.S.) in
Clinical and Chemical Pathology

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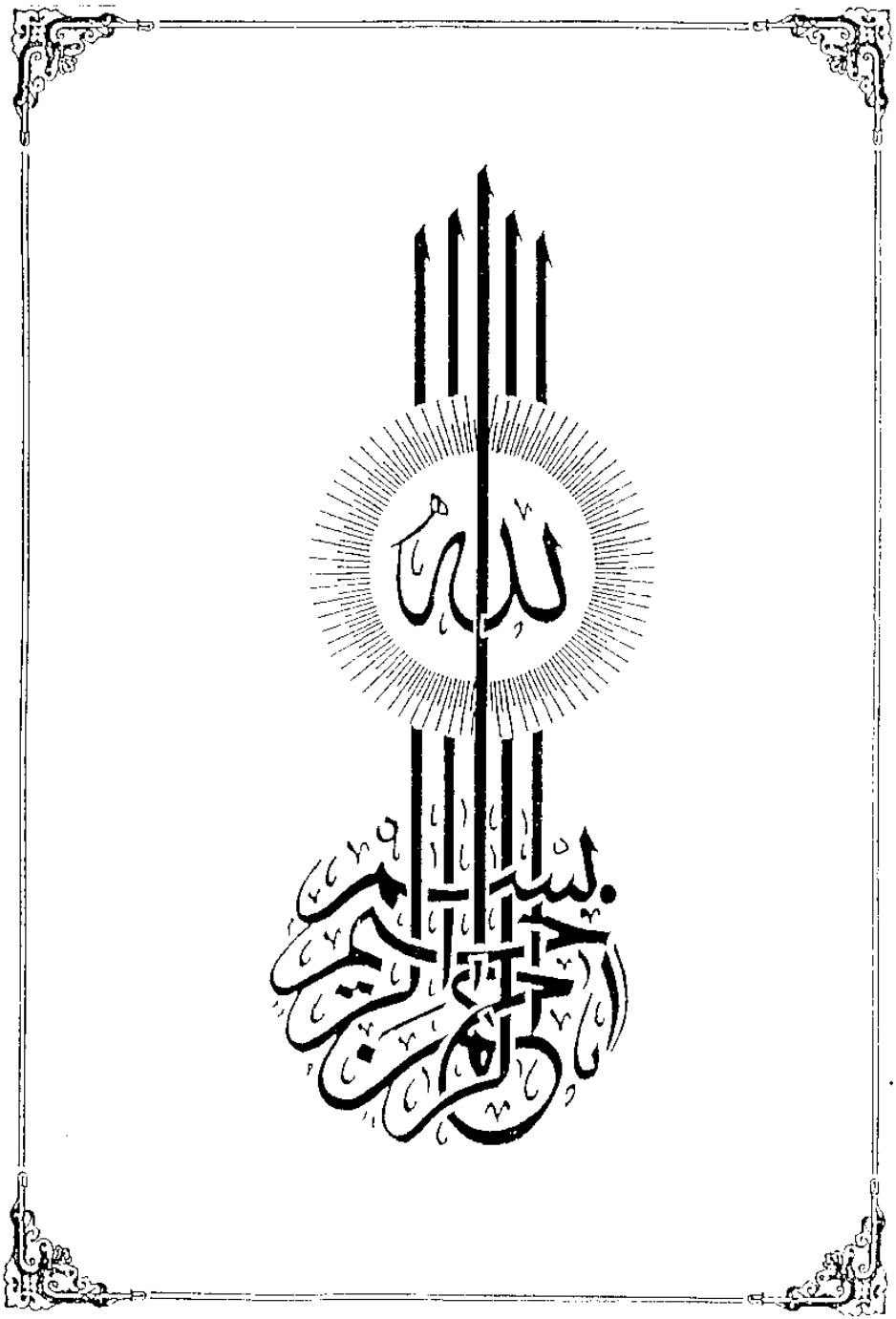
1989

قالوا

سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة الآية ٣٢



ACKNOWLEDGEMENT

I would like to express my deep thanks and gratitude to Dr. Alya Sadek Moustafa, Assistant Professor of clinical pathology, Faculty of medicine, Ain Shams University for her valuable help and considerable support.

I would like to express my deep thanks and gratitude to Dr. Zeinab Mohamed Tawfik, Assistant Professor of clinical pathology, Faculty of medicine, Ain Shams University, for her instructive supervision, suggestions and guidance.

I am also greatly grateful to Dr. Bassima Mahmoud Ahmed, Lecturer of clinical pathology, Faculty of medicine, Ain Shams University, for her valuable help and sincere effort.

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ABBREVIATIONS

* AIDS	:	Acquired immunodeficiency syndrome
* ASO	:	Anti streptolysin "O".
* CGD	:	Chronic granulomatous disease.
* CNSHA	:	Chronic non spherocytic haemolytic anaemia.
* C.S.F	:	Cerebrospinal fluid
* E.Coli	:	Escherichia coli
* G-6-PD	:	Glucose-6-Phosphate dehydrogenase
* HAV	:	Hepatitis "A" virus
* HBsAg	:	Hepatitis B Surface antigen
* HBV	:	Hepatities B virus
* H. Influenza	:	Haemophilus influenza
* HIV	:	Human immunodificiency virus
* HMP	:	Hexose monophosphate
* HPV	:	Human Parvo virus
* H.S	:	Hereditary spherocytosis
* LAV	:	Lymphadenopathy virus
* NBT	:	Nitro blue tetrazolium
* NK	:	Natural Killer
* PMN	:	Polymorphonuclear
* PNH	:	Paroxysmal nocturnal haemoglobinuria
* RES	:	Reticulo endothelial system

* S.C.A. : Sickle cell anaemia.
* S.C.D : Sickle cell disease
* SIg : Secretory immunoglobulin
* UIBC : Unbound iron binding capacity.

INTRODUCTION AND AIM OF THE WORK

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The association of haemolytic anaemia with increased susceptibility to serious infections has been recognized and studied. Infection and not crisis is the most common cause of death in patients with sickle cell anaemia, and many hypothesis suggest that infection commonly precipitates crisis (Barrette-Conner, 1971), moreover prevention of febrile disease by regular doses of long acting penicillin reduces clinical crisis and improves the haematological picture in children with sickle cell anaemia. The infections affecting persons with sickle cell anaemia include pneumococcal pneumonia and salmonella (Adeyokunnu and Hendrickse, 1980), haemophilus influenza (Ward and Smith, 1984) and streptococcus infection (Mollouh and Salamah, 1985), some of these infections are attributed to an opsonophagocytic defect due to an abnormality of the alternate pathway of complement activation, a state of functional hyposplenia and lack of specific circulating antibodies as a developmental phenomenon (Pearson, 1971). Abnormal leucocytic function and abnormal reticuloendothelial system function have been proposed as the cause of crisis for this unique susceptibility (Mollouh and Salamah, 1985).

Patients with thalassemia major are at risk of virus infection especially when have frequent blood transfusion (Lefrere and Girot, 1987), others are more susceptible to enterocolitica sepsis (Chiesa et al., 1987) and pseudo tuberculosis septicaemia (Gordts et al., 1984).

Moreover, patients with glucose-6-phosphate dehydrogenase deficiency have been reported to have increased susceptibility to infection similar to that of chronic granulomatous disease of childhood with an increased susceptibility to infection by catalase-positive bacteria, chemotaxis and phagocytosis are normal but there is defective bactericidal activity of the leucocytes (Mamlok et al., 1987).

The aim of this work is to review the incidence, cause and type of infections in patients with haemolytic anaemias associated with infection and methods of preventing overwhelming infection in these patients if possible.

HAEMOLYTIC ANAEMIAS

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The fundamental basis of the haemolytic anaemias is a shortened survival time of red blood cells. RBCs normally spend 100 - 120 days in the circulation, about 1 % of red cells (senescent ones) are removed from blood each day and are replaced by an equal number of new cells released from the bone marrow (Erslev 1967).

In response to a shortened survival of red cells, the activity of bone marrow increases. The peripheral reticulocytic count exceeds 2 %. Sustained reticulocytosis in conjunction with unchanging haemoglobin level is presumptive evidence of a haemolytic disorder (Oski, 1981).

Hyperplasia of the erythropiotic marrow elements occurs, with lowering or reversal of the myeloid-erythroid ratio. Elevation of unconjugated bilirubin may accompany many haemolytic states, but overt Jaundice is unusual if hepatic function is not impaired. Accelerated destruction of red cells increases the biliary excretion of haem pigments, which can be quantitated by measurement of fecal urobilinogen (Schmid 1978).

Plasma concentrations of haemoglobin increase in haemolytic anaemias, and the free Hb combines irreversibly

with haptoglobin. The large haptoglobin-haemoglobin complex is cleared from the circulation by reticulo-endothelial activity. In severe haemolytic states, the loss of haptoglobin exceeds the synthetic capacity of the liver and serum haptoglobin is decreased or absent (Nagel and Gibson 1971). The level of hemopexin, another plasma protein that binds Hb, is also reduced in haemolytic states.

Classification of Haemolytic Anaemias (Oski, 1981):

I- Hereditary Haemolytic Anaemias:-

1- Hereditary spherocytosis
2- Hereditary elliptocytosis
3- Thalassaemias.
4- Haemoglobinopathies
5- Enzyme deficiency haemolytic anaemias.

II- Acquired Hamolytic Anaemias:

1- Immune haemolytic anaemias:
   a- Autoimmune haemolytic anaemias (AIHA)
   b- Alloimmune haemolytic anaemias
   c- Drug-Induced haemolytic anaemias

2- Drug-induced haemolytic anaemias (non-immunologic mechanisms):

a- Direct toxic effect

b- Idiosyncrasy mechanism

3- Haemolytic anaemias associated with numerous irregularly contracted erythrocytes in the blood film.

- Mechanical haemolytic anaemia
- Microangiopathic haemolytic anaemias

4- Paroxysmol nocturnal haemoglobinuria

5- Miscellaneous:

Infectious agents (uncommon)

Protozoal parasites malaria.

Bacteria : clostridium welchii.

Hereditary Spherocytosis: (HS):

This is a familiar disorder characterized by the presence of spherocytes in the peripheral blood, a shortened red cell life span, splenomegaly and cure of haemolysis by splenectomy (Emerson et al., 1947).

The usual mode of inheritance is autosomal dominent though in about quarter of cases, there is no family history. (Morton et al., 1962).

It seems probably that there is an abnormality of structure of the red cell membrane in HS. Membrane lipids are present in normal proportions, though the absolute amount per cell may be reduced. This suggests that membrane is lost intact from the cells rather than there being any abnormality of lipid production. (Reed and Swisher, 1966). Also, there have been suggestions that there is an abnormality of a structural protein in HS cell membrane, and there is some tentative evidence to support this hypothesis (Hayashi, 1974).

There is an increased permeability to sodium, this is balanced by an increase in active transport of sodium ions outwards which requires an increased energy supply, provided by glycolysis, so HS cells are abnormally dependant on glucose (Wiley, 1972).

The spleen plays an essential role in the pathogenesis of haemolysis in HS. The cells are more rigid, this prevents normal passage through the slit-like opening seperating splenic cords from sinusoids. This delay will result in prolonged period of hypoxia which compromise the RBCs metabolism resulting in loss of cell membrane, more sphering and rigidity. Furthure passage through spleen