NON-SALMONELLA BACTERAEMIA PRESENTING AS FEVER OF UNDETERMINED ORIGIN

THESIS

SUBMITTED IN PARTIAL FULFILMENT

OF THE MASTER DEGREE IN

(TROPICAL MEDICINE)

By

Salwa Yousef Safwat

M.B., B.Ch.

SUPERVISED BY :

Prof.Dr. Mohamed F. Abdel-Wahab

Prof. of Tropical Medicine

Faculty of Medicine

AIN SHAMS UNIVERSITY

Dr. Zoheir Farid

Prof. & Head of

Tropical Medicine

Dept., Namru-3

Dr. Mohamed Fawzy Montasser

Lec. of Tropical Medicine

Faculty of Medicine

AIN SHAMS UNIVERSITY

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

1986

ACKNOWLEDGEMENT

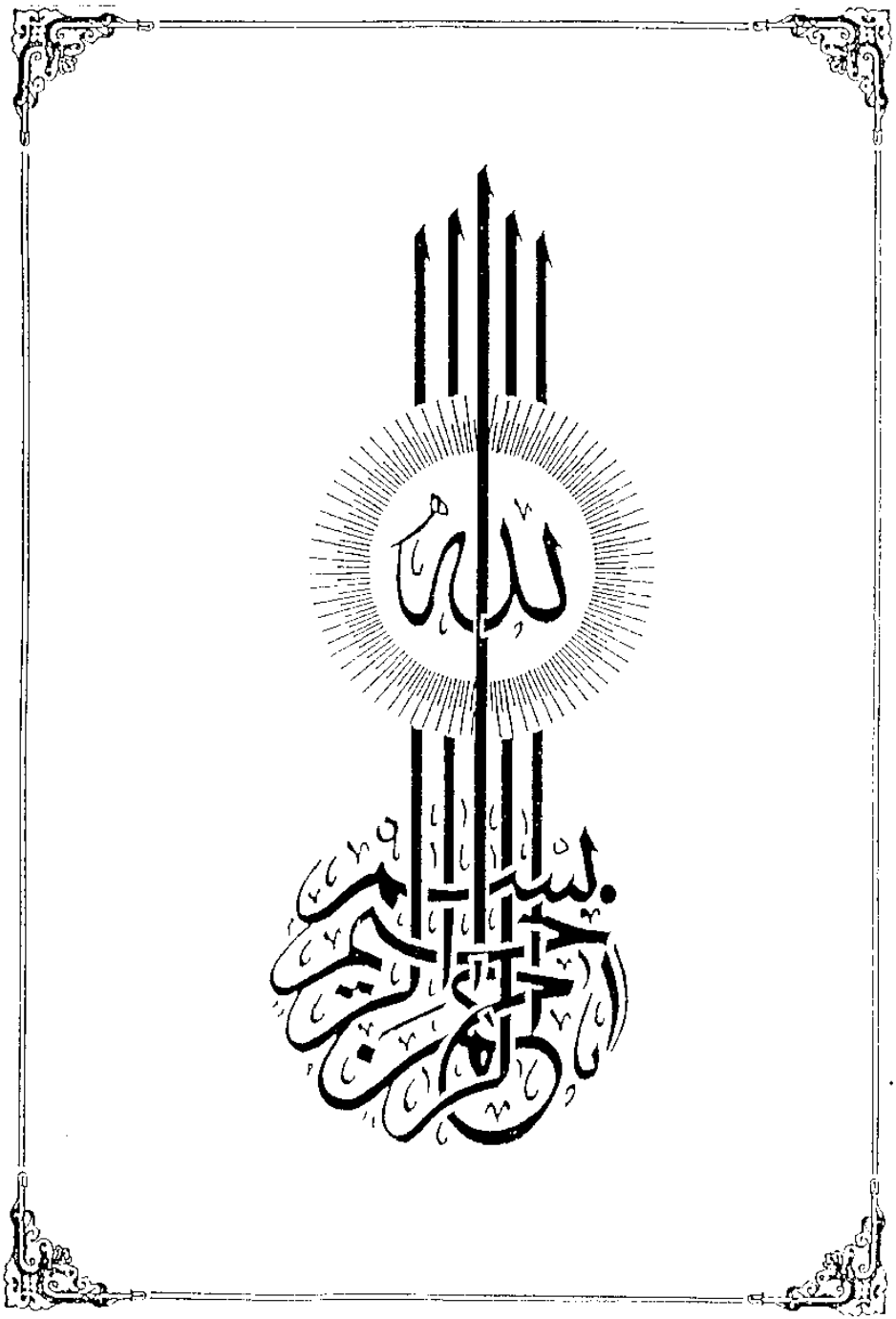
I would like to express my deepest gratitude to **Prof. Dr. SALAH SAIF EL-DIN,** Professor and Head of Department of Tropical Medicine, Ain Shams University for his continuous support throughout the study.

I am indebted to **Prof. Dr. MOHAMED FATHY ABDEL WAHAB,** Professor of Tropical Medicine, Ain Shams University and **Dr. ZOHEIR FARID,** Head of Tropical Medicine Department, Namru-3 for suggestion, continuous revision, patience and kind guidance throughout the work.

Thanks to **Dr. MOHAMED FAWZY MONTASSER,** Lecturer of Tropical Medicine, Ain Shams University for his valuable advice and criticism.

I wish to express much thanks to **Dr. YOUSEF SAFWAT,** Senior Fever Consultant in Abbassia Fever Hospital for his utmost help, guidance and revision of this work.

The great help of **Dr. ABDALLA HAFEZ,** Director General Abbassia Fever Hospital, **Dr. FATMA SAID,** Specialist Abbassia Fever Hospital and **Dr. BESHARA GORGE EL TARABOLSI,** Specialist Abbassia Fever Hospital for their kind help and advice in the practical part of the work.



Lastly, I am grateful to every one who participated in the evolution of this work.

CONTENTS

---oooOooo---

INTRODUCTION
&
AIM OF THE WORK

INTRODUCTION

AND

AIM OF THE WORK

Bacterial infections represent the commonest cause of fevers of undetermined origin (F.U.O.) in Egypt. During a ten years (1975-1984) study of 699 F.U.O. cases in Abbassia Fever Hospital, 307 (43.92%) patients were due to intectious cause.

Among the various forms of bacterial infections, bacteraemia preserves a special consideration because there is a steady increase in the incidence of gram negative bacteraemia with the potential danger of bacterial shock with its disastrous effect on the life of the patients **(Mc Cabe et al., 1972).**

The aim of this work is study cases of non-salmonellae bacteraemia presenting as F.U.O. from the clinical, laboratory and therapeutic point of view.

REVIEW OF LITERATURE

FEVER OF UNDETERMINED ORIGIN IN EGYPT

Fevers of undetermined origin (F.U.O.) or pyrexia of unknown origin (P.U.O.) or cryptogenic fever is a clinical problem encountered in medical and surgical practice. Sheon and Ommon (1963), defined F.U.O. as a temperature higher than 100.5°F, persisting for at least 3 weeks in patients in whom history, physical examination, blood count, urine analysis and chest x-ary film do not indicate the diagnosis.

Bulmer (1943), working in a military hospital in Egyptian desert reported on 2000 F.U.O. cases. Most of the cases proved to be short term fevers as malaria, enterica, meningitis relapsing fever or dysentry. Of the remaining 1153 cases, 805 were most probably sandfly fever and 348 remained undiagnosed.

Gravey (1950), reported on 30 F.U.O. military patients in Egypt. He found that most of them were short term fevers as malaria, sandfly fever, reespiratory infections, typhoid, typhus and amoebic hepatitis.

El-Rooby (1959), studied 46 F.U.O. cases and found that 29 (63%) remained undiagnosed, 17 (37%) were diagnosed as tuberculosis, brucellosis, amoebic

hepatitis, typhus, typhoid urinary carrier, chronic apendicitis, rheumatic fever, subacute bacterial endocarditis, leukaemia, supra renal neurocytoma, cavernus sinus thrombosis and Shonlein Henoch syndrome.

Mohran (1973), studied 90 patients with P.U.O. admitted over a 10-year period to Ain Shaims University Hospital, Cairo. Infections particularly parasitic diseases and local infections were the most frequent causes of F.U.O. (45%). Neoplasms came second (20%) with lymphomata as a major subdivision. Blood dyscrasias accounted for 7%, collagen diseases, chronic active hepatitis and paroxysmal allergic peritonitis for 5% each and intestinal diseases for 3% while 9% remained undiagnosed.

The first well documented study on F.U.O. in Egypt was started in 1971 in Abassia Fever Hospital, Cairo. During the period 1971-1973, 129 F.U.O. patients fulfulling Sheon's criteria (1963) were included in the study (Hassan and Farid, 1974). Out of these 129 F.U.O. cases, 78 (60%) were due to infections (salmonellosis, tuberculosis, brucellosis, pyelonephritis, sepsis, malaria, kala-azar and leprosy), 18 cases (14%) due to neoplasms (lymphoma, leukaemia, dissiminated carcinomatosis, localised tumour and multiple myeloma), 13 cases (10%) due to collagen disease (rheumatic fever,

dissiminated lupus erythematosis and rheumatoid arthritis), 4 cases (3%) other causes and 16 cases (13%) remained undiagnosed. A striking observation from this study, was that over two thirds of the patients had received several courses of antibiotic therapy and about one third had corticosteroid therapy resulting in masking the clinical picture and delaying the exact diagnosis.

Infections (60%) are still the commonest cause of obscure fever in Egypt especially salmonellosis, tuberculosis, and urinary tract infections.

Maltreated typhoid and chronic salmonellosis headed the list of infections in Egypt.

Maltreated typhoid patients usually receive interrupted or incomplete underdosaged antibiotic therapy resulting in slight amelioration of the general condition of patient with persistence of fever (Hassan, 1974). Repeated blood cultures and serial widal agglutination test usually clinch the diagnosis.

Chronic salmonellosis presents a clinical entity of salmonella infection quite different from classical enteric fever, characterised by prolonged fever and bacteraemia in bilharzial patients. Two forms of chronic salmonellosis have been described in Egypt.

(1) Chronic salmonellosis complicating S-haematobium infection (Hathout et al., 1967, and Farid et al., 1970). The patients usually complain of remittent or intermittent type of fever of long duration (1-24 months) with frequent chills. dysuria and hematuria are common symptoms. Toxicity is not characteristic of the disease. Hepatosplenomegaly is not uncommon. The liver may be enlarged and tender misdiagnosed as amoebic hepatitis or viral hepatitis. No significant tympanitis or tenderness of the abdomen is elicited. Repeated blood and urine cultures usually reveal S-paratyphi A (five fold) or S-typhi. Most of the cases have normal white blood count and low or moderately elevated widal titres. Urine examination usually reveals S-haematobium ova. Intravenous pyelography usually shows damaged urinary tract and evidence of obstructive uropathy.

(2) Chronic salmonellosis complicating S. mansoni infection (Bassily et al., 1977 and Abdel-Wahab et al., 1977). The clinical picture of the disease is that of reticuloendotheliosis. The patients usually complain of irregular type of fever of long duration (1-24 months), frequent attacks of chills and diarrhoea. Anorexia, epistaxis, loss of weight and abdominal pain are common. The patients, look

toxic, pale and emaciated. Generalised lymphadenopathy is common.

Significant hepatospenomegaly is a constant feature. Ascites and jaundice are not uncommon. Oedema of the lower limbs, petechial rash and purpuric eruptions are usually elicited. Positive blood cultures, anemia, thrombocytopenia and raised erythrocyte sedimentation rate are constant findings.Stool usually shows S. mansoni ova. Combined antityphoid and antibilharzial therapy should be administered to eradicate the infection in chronic salmonellosis.

Tuberculosis especially its extrapulmonary form is an important cause of F.U.O. Molavi and Weinstein (1970), reported that the liver, peritoneum, pericardium, bone, lymphnodes and female genital tract are the main sites of extrapulmonary tuberculosis causing F.U.O. Prolonged fever, coagh, abdominal discomfort, anorexia and loss of weight are suggestive findings. Anaemia, significant rise of erythrocyte sedimentation rate, negative tuberculin test and normal chest x-ray films are the usual laboratory findings (Safwat et al., 1976). Cervical glands are a common site of tuberculous lymphadenitis (Warraki, 1970), followed by abdominal and hilar ones. Urinary tuberculosis may have an extremely slow onset and much destruction to the kidneys can

result before overt symptoms and signs are elicited. Sterile pyuria and unexplained hematuria may be the earliest signs of urinary tuberculosis (Citron, 1973). Fever, abdominal pain, night sweats, weight loss and tender doughy abdomen with or without slight ascites appear to be the main symptoms and signs of tuberculous peritonitis **(Fedotin and Brewer, 1972).**

Petersdorf and Beeson (1961), and Safwat et al. (1976), stressed the importance of early histological examination of tissues (lymph node examination and liver biopsy) in reaching a diagnosis in patients with obscure fever. 5 out of 8 F.U.O. patients with extra-pulmonary tuberculosis (tuberculous lymphadenitis, peritonitis, granulomatous hepatitis and renal tuberculosis) revealed negative routine investigations and were diagnosed only by tissue biopsy **(Safwat et al., 1976).**

Urinary tract infections present a challenging diagnostic and therapeutic problem.

Clinically there may be attacks of pain in one or both loins, fever, rigors, dysuria, frequency and turbidity of urine. The condition may be asymptomatic or poorly presented in the form of unexplained fever or ill health (El-Said, 1972). Routine repeated urine

culture and sensitivity is important in cases of F.U.O. especially in females and children.

Farid et al.(1977), studied 12 cases of hepatic amebiasis in Cairo presenting as F.U.O. during the period 1971-1976. The liver was enlarged and tender in 7 cases. Haemoglobin was under 10gms/100ml. in 8 patients and leukocyte counts of over 10000mm^3 in nine. In 8 of 9 patients in whom it was performed, counterimmunoelectrophoresis serologic test was positive and was the first indicating the diagnosis. In these patients, indirect hemagglutination and immunodiffusion later proved positive as well. Chest radiographs revealed right diaphragmatic pleurisy in 7 cases. In 4 patients in whom liver scan was performed, a defect was elicited.

Neoplasms come next to infections as a cause of F.U.O. lymphomas and leukaemia are the commonest forms of neoplasm encountered in F.U.O. Fever, loss of weight, anemia, high erythrocyte sedimentation rate are usually elicited. Lobell et al. (1966), studied 137 patients with histologically proven hodgkin's disease and found that 50% of the cases eventually developed fever of non-infectious etiology during the course of their disease whereas only 13% developed fever due to infection. Bone marrow examination, tissue biopsy