Incidence of Cryptosporidium in Patients with Chronic Liver Disease with Recurrent Diarrhea

Thesis Submitted for Partial Fulfilment
of Master Degree in Tropical Medicine

BY
Sherif Farouk Ali Metwaly
(M.B., B.Ch.)

UNDER SUPERVISION OF

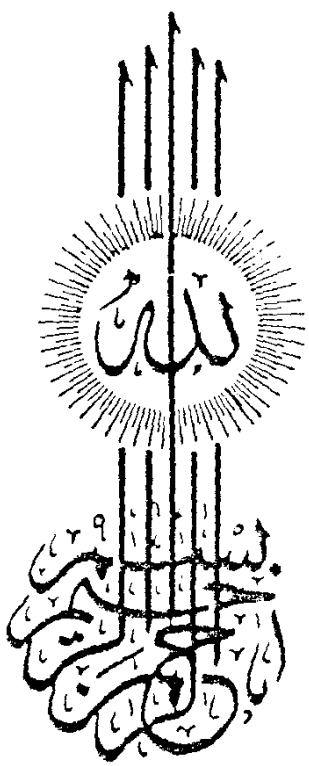
Prof. Dr. Mubarak Mohamed Hussein
Professor of Tropical Medicine
Ain Shams University

Dr. Tayseer Aly Younis
Ass. Prof. of Parasitology
Ain Shams University

Dr. Sanaa Moharram Ahmed Kamal
Lecturer of Tropical Medicine
Ain Shams University

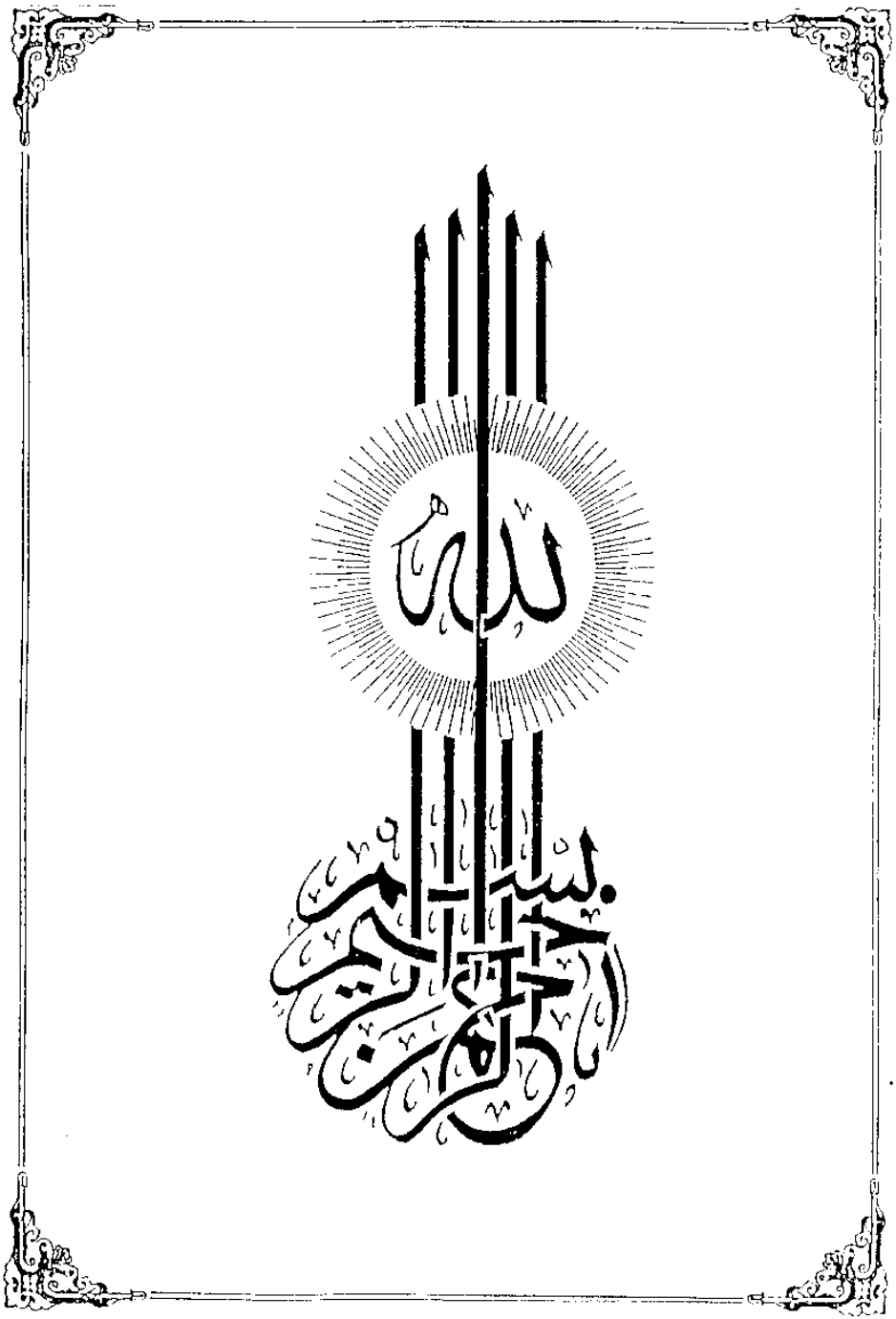
FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

1995



وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ

«صَدَقَ اللهُ العَلِيمُ»



ACKNOWLEDGEMENT

I am indebted to **Prof. Dr. Mohammad Ali Madwar**, Head of the Tropical Medicine Department, Faculty of Medicine, Ain-Shams University, for his support and encouragement.

I wish to express my deep gratitude to **Prof. Dr. Mubarak Mohamed Hussein,** Prof. of Tropical Medicine, Ain-Shams University, for his fatherly attitude in supervising, guiding and supporting me throughout the whole work. His witty hints and encouragement have been a real help in performing this study.

I owe much to **Dr. Sanaa Moharram Kamal**, Lecturer of Tropical Medicine, Ain-Shams University, for her patience and perseverance. She has generously devoted much of her time and provided detailed criticism and unlimited support which have been a real help in accomplishing this study. Such an enormous effort is cordially appreciated.

I am also very grateful to **Dr. Tayseer Aly Younis,** Assistant Prof. of Parasitology, Faculty of Medicine, Ain-Shams University, for her generous time and kind supervision during the laboratory part of this work.

Thanks and gratefulness to **Dr. Doreya Mohsen Mahmoud,** Lecturer of Parasitology, Faculty of Medicine, Ain Shams University, for her valuable cooperation and kind assistance throughout the work.

It is pleasure to express my thanks to the staff members and residents of Tropical Medicine Department, Ain-Shams University, for their kind help.

CONTENTS

○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○

INTRODUCTION AND AIM OF THE WORK

INTRODUCTION AND AIM OF THE WORK

Introduction:

Cryptosporidiosis is a diarrheal disease produced by protozoa of the genus Cryptosporidium (Plorde et al, 1990).

These parasites inhabit the microvillus border of the intestinal epithelium where they produce clinical illness ranging from an acute severe, self limited, watery diarrhea in normal individuals to chronic, severe life - threatening gastro-enteritis in immunocompromised individuals (D'Antonio et al, 1988).

The first cases of human cryptosporidiosis were reported in 1976 (Miesel et al, 1976, Nime et al, 1976), and subsequent reports were rare until it was recognized as an important enteric pathogen especially in immune deficient patients (Fayer and Ungar, 1986).

Cryptosporidia now rank with Salmonella, Shigella, Campylobacter, enterotoxigenic E. coli and Giardia lamblia as major pathogens of humans (Janosff and Reller, 1978).

Most forms of chronic liver disease are accompanied by depressed immune response (Soave, 1988). Hypoglobulinemia

and depressed cell mediated immunity are common in various forms of chronic liver disease where the immunological derrangements run parallel to the extent of liver damage. (Ungar et al, 1986). Hepatic cirrhosis is characterized by altered handling of antigens due to depression of both humoral and cell mediated immunity (Colley et al, 1988).

Schistosomiasis and viral hepatitis represent the most common etiologies of liver disease in Egypt and both have a direct suppressive effect on the immune system with marked inability of handling invading pathogens (Kojime et al, 1984).

Patients with chronic liver disease, especially in advanced stages are liable to a wide spectrum of bacterial, viral and parasitic infections (James, 1986).

The immune status of the host appears to be the major factor determining the severity and duration of infection following oral exposure to Cryptosporidium Oocysts (Ungar et al., 1988).

Cryptosporidiosis should be considered with differential diagnosis of recurrent attacks of diarrhea in patients with chronic liver disease. Since persistent and severe diarrhea may have serious consequences in patients with advanced liver

disease, cryptosporidiosis should be properly diagnosed early to be treated adequately.

Aim of the Work

The present study is designed to study the incidence of Cryptosporidium in patients with various stages of Schistosomal and/or posthepatitic liver disease presenting with recurrent attacks of diarrhea.

REVIEW OF LITERATURE

CHAPTER I
Cryptosporidiosis

HISTORY AND TAXONOMY

Organisms of the genus Cryptosporidium are small (2-6 μm, depending on stage of life cycle) coccidian parasites which invade and then replicate within the microvillous region of epithelial cells lining the digestive and respiratory organs of vertebrates (Angus 1983, Current 1986, Fayer & Ungar 1986, and Tzipori 1983).

Recognized and named more than 80 years ago (Tyzzer 1912), these obligate intracellular protozoans remained until recently nothing more than a biomedical curiosity. Prior to 1980, infections with species of Cryptosporidium were considered rare in animals and in man they were thought to be the result of a little-known opportunistic pathogen of immune-deficient individuals outside its normal host range. In 1982, the concept of these protozoan parasites began to change into that of important, wide spread causes of diarrheal illness in several animal species, including humans. The finding of this parasite in the immuno compromised host, especially patients with AIDS, usually carries an ominous prognosis. Reports of infections of the respiratory tract (Forgacs et al,

1983) and biliary tree (Pitlik et al, 1983) demonstrate that the developmental stages of this protozoan are not confined to the gastrointestinal tract and suggest that Cryptosporidium parvum may be an under reported cause of respiratory and biliary tract disease, especially in the immune-deficient host.

Recent recognition of the importance of Cryptosporidium species as pathogens of man and his domesticated animals can be confirmed easily by the number of relevant publications that have appeared in the biomedical literature. Fewer than 30 papers addressing these parasites were published prior to 1980; however, currently, more than 630 papers on Cryptosporidium species and cryptosporidiosis exist. Among the many recent papers are several reviews of the biology of Cryptosporidium species infecting man and his domesticated animals (Current 1986; Fayer and Ungar, 1986, Crawford & Vermund, 1988).

Clarke (1895) may have been the first to observe a species of Cryptosporidium which he described as 'swarm spores lying upon the gastric epithelium of mice'. In retrospect, these small organisms were probably the motile merozoites of Cryptosporidium muris, the type species named and described approximately 12 years later by the well-known American parasitologist, E.E. Tyzzer (1907). This protozoan, infecting the

gastric epithelium of laboratory mice used in Tyzzer's research programme, was placed in a new genus (Cryptosporidium = hidden sporocysts) because, unlike the previously known coccidia, the oocyst of this parasite did not have sporocysts surrounding the sporozoites. Three years later, Tyzzer (1910) described many of the life-cycle stages of Cryptosporidium muris and in 1912 he described much of the morphology and life cycle of a second species, Cryptosporidium, found in the small intestine of laboratory mice (Tyzzer, 1912). During the ensuing 70 years, approximately 19 additional species of Cryptosporidium were named from a variety of vertebrate hosts (Le Vine, 1984, Current, 1986; Fayer & Ungar, 1986). Only a few of these named species, including the two originally described by Tyzzer, are now considered valid (Table A).

Interest in Cryptosporidium parvum by the veterinary medical profession has increased significantly since 1971 when this protozoan was first reported to be associated with bovine diarrhea (Panciera et al, 1971). Numerous case reports from many different animals are now present in the literature and one species, Cryptosporidium parvum, is recognized as an important cause of neonatal diarrhea in calves and lambs (Angus 1983, Tzipori, 1983 and Current, 1986).

Another species, Cryptosporidium baileyi, is now

recognized as an important cause of respiratory disease in poultry (Current et al, 1986; Blagburn et al, 1987; Current & Synder, 1988). The first cases of human cryptosporidiosis were reported in 1976 (Miesel et al, 1976; and Nime et al, 1976), and subsequent reports were rare until it was recognized that Cryptosporidium (now believed to be Cryptosporidium parvum) may produce a short-term diarrheal illness in immunocompetent persons and a prolonged, life-threatening, cholera-like illness in immune-deficient patients, especially those with acquired immune deficiency syndrome (AIDS) (Current et al, 1983; Current, 1986; and Fayer & Ungar, 1986).

The taxonomic classifications of small intracellular protozoans assigned to the genus Cryptosporidium is presented in table B.