A STUDY OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH ASCITES DUE TO LIVER CIRRHOSIS

THESIS

SUBMITTED FOR PARTIAL FULFILMENT OF THE DEGREE OF M.S. IN GENERAL MEDICINE

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1987

ACKNOWLEDGEMENT

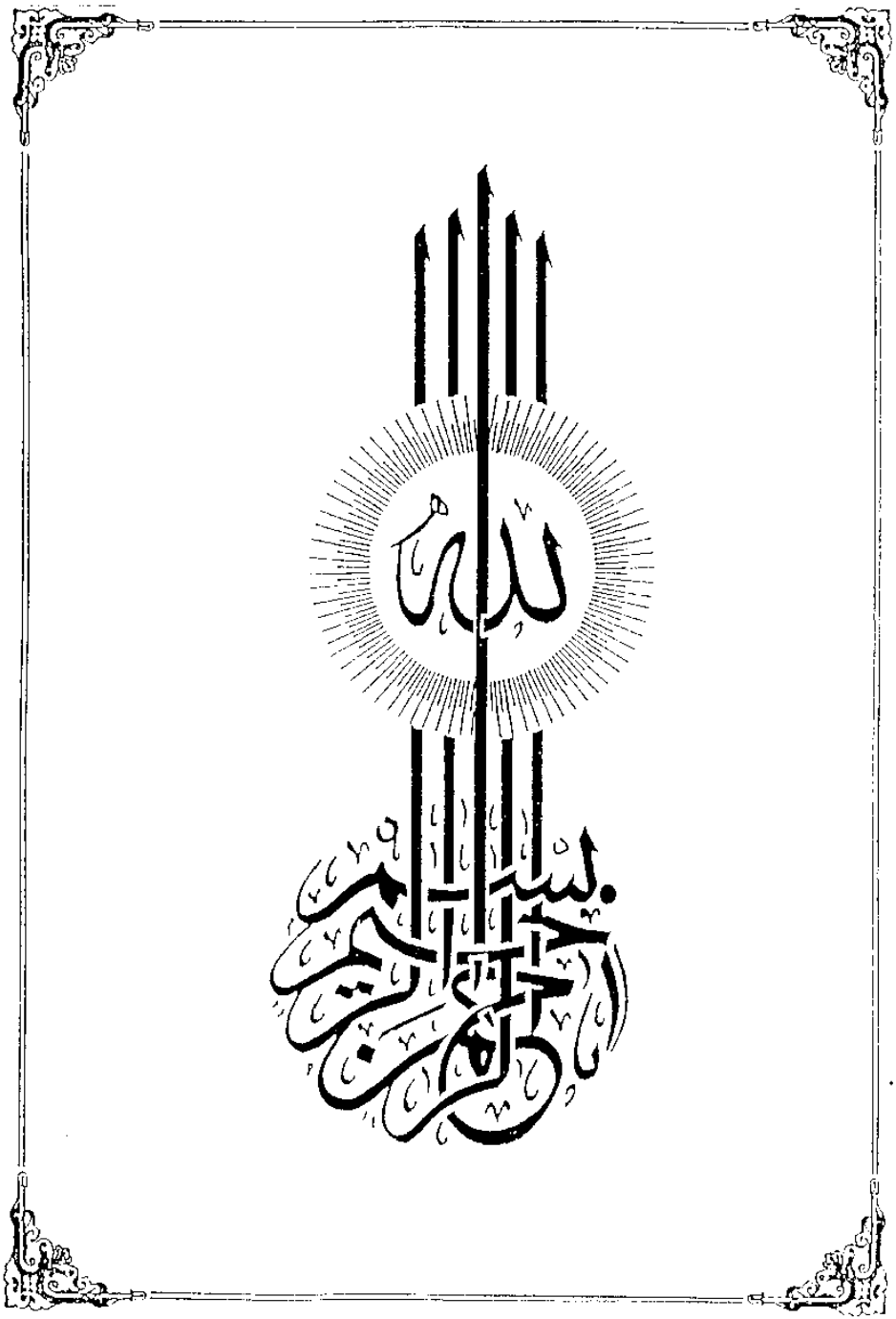
(THANKS TO GOD)

I would like to express my deepest gratitude and cordial thanks to Prof. Dr. MOHAMMAD SADEK SABBOUR, Professor and Head of the Department of Medicine, Ain Shams University, for his kind advice, constant encouragement and fruitful criticism.

I owe special gratefullness and much regards to Prof. Dr. LAILA OSMAN, Professor and Head of the Department of Clinical Pathology, Ain Shams University, for her warm kindness, understanding, real help and continuous guidance throughout this work.

I would like also to thank Prof. Dr. TAHANY ABD EL HAMEED, Professor of Microbiology, Ain Shams University, for her help and guidance.

Lastly, thanks for all who have helped in the accomplishment of this work, and best wishes for all the patients.



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Spontaneous bacterial peritonitis (SBP) is defined as infected ascitic fluid without any apparent intra-abdominal foci of sepsis. It is an often fatal complication of cirrhosis. It is thought that ascites is a *sine qua non* of this syndrome.

In view of the high mortality (43-70%), early diagnosis and treatment are imperative (Curry et al., 1974; Hoefs et al., 1982).

A positive bacteriological culture of the ascitic fluid is the "Gold Standard" for the diagnosis. However, it requires 24-72 hours before a positive culture can be obtained. Raised values of ascitic fluid leucocytic count and plymorphnuclear cells are accepted as "Silver Standard" for the diagnosis.

THE AIM OF THIS WORK:

I. To estimate the real size of spontaneous bacterial peritonitis (SBP) among Egyptian patients with ascites due to liver cirrhosis, and to compare between the efficacy of different laboratory tests in the early diagnosis of this syndrome. These tests include the following:

1. Bacteriological examination of the ascitic fluid.
2. Total and differential white blood cell counts of the ascitic fluid.
3. Ascitic fluid pH level.

4. Total lactic dehydrogenase level of the ascitic fluid.
5. Total proteins concentration of the ascitic fluid.

II. To put a spotlight on culture negative neutrocytic ascites (CNNA) as a variant of spontaneous bacterial peritonitis (SBP).

III. To make a review on published works on ascites and spontaneous bacterial peritonitis (SBP).

REVIEW OF LITERATURE

ASCITES

Definition

Ascites refers to accumulation of abnormal volumes of free non-purulent fluid within the peritoneal cavity.

Historical Background

The term ascites was derived from Greek word askos, meaning a bag.

Historical evidence indicates that the Egyptians, 1500 B.C., were aware of abnormal collections of abdominal fluid associated with diseases of the liver (Hyatt and Smith, 1954).

Hippocrates recognised an association between liver disease and dropsy, he stated that "when the liver is full of fluid and this overflows into the peritoneal cavity so that the belly becomes full of water, death follows" (Dawson, 1960).

Erasistratus of Alexandria (250 B.C.) postulated that ascites was due to the stone-like hardness of the liver, commenting that "the blood is prevented from going forward into the liver owing to the narrowness of the passage."

Celsus, 20 B.C., gave a detailed description of paracentesis as a line of treatment of ascites, though he believed that trial of medical therapy should be made before one resorted to it (Dawson, 1960).

Peritoneal Fluid and Ascites

The adult peritoneal cavity contains normally from 100 to 200 ml of free non-purulent fluid. Ascites refers to accumulation of abnormal volumes of free non-purulent fluid within the peritoneal cavity.

Ascites is not a disease in itself but a manifestation of many diseases of various organs. In absence of a local cause, and if it is associated with hepatocellular disease, ascites implies liver cell failure and portal hypertension.

It complicates all forms of cirrhosis and implies a poor prognosis (Ratnoff and Patek, 1942).

Cardiac cirrhosis or any form of hepatic venous obstruction results in considerable ascites.

It is usually demonstrable clinically when 500 ml or more of fluid has accumulated in the peritoneal cavity (Trisdale et al., 1974).

Ascites-plasma Interchange

Ascites is not a static pool of fluid but it is in dynamic equilibrium with the plasma. It is a continuously circulating fluid, half of the amount present leaves and enters the peritoneal cavity every hour, there being a rapid transit in both directions (Birkenfeld et al., 1958).

Prentice and his colleagues (1952) had shown that the water content of the ascites is exchanged with that

of blood at a rate of 40-80% each hour. Ascites forms when the rate of fluid entering the peritoneal cavity exceeds the rate leaving it. The proteins of ascitic fluid also readily interchange with those of the plasma and this is known as dynamic equilibrium.

Both albumin and globulin participate in the interchange between blood and ascites, albumin turnover is three times more rapid than that of globulin (Mckee et al., 1952). Labelled albumin appears in ascitic fluid approximately 30 minutes after I.V. injection of labelled substance and vice-versa (Shoenberger et al., 1952). Albumin diffuses from plasma to ascitic fluid at a rate of 4 per cent per hour. This is why intravenous albumin infusions increase the ascitic fluid albumin concentration without conspicuously raising the serum albumin level, and serum albumin rises when intraperitoneal albumin is administered (Shoeb, 1959).

The fluid exchange between ascitic and vascular compartment is mainly through the visceral peritoneum. Once formed, ascitic fluid can exchange with blood through the enormous capillary bed under the visceral peritoneum.

Peritoneal permeability is an important factor in ascites production (Mankin and Lowell, 1948). Peritoneal permeability increased in cases of liver cirrhosis, because of increased capillary permeability, probably due to associated malnutrition. If the patient nutritional state is

improved and his plasma protein level is corrected, peritoneal permeability decreases and albumin no longer passes into ascitic fluid (Kark, 1951).

Pathogenesis

Theoretically, ascites represents a local consequence of an imbalance of those factors which favor the exudation of fluid from the vascular compartment over those which maintain vascular volume. Starling in 1896 suggested that the transudation of fluid between capillaries and tissue spaces was determined by the equilibrium of hydrostatic and osmotic factors in the two compartments (Sherlock, 1985).

Several disorders of hydrostatic and osmotic equilibrium within the body can be identified in hepatic disease when ascites accumulates.

The constituents of the ascitic fluid are in dynamic equilibrium with those in plasma.

Movements of material between the abdominal cavity and circulation are modified by lymphatic system and mediated by peritoneal membrane. Both intra-abdominal and systemic factors are involved in ascites formation, intra-abdominal factors localize accumulation of fluid mainly within the abdomen, whereas systemic factors causes retention of sodium and water throughout the body.

So, this interaction between both intra-abdominal and systemic mechanisms (which include hormonal, metabolic,

renal and circulatory adjustments) are generally invoked to explain the pathogenesis of ascites.

I- Intra-abdominal Factors

According to Starling law of equilibrium, osmotic and hydrostatic forces determine movement of fluid from portal capillary circulation to the interstitial space and peritoneal cavity.

Normally, the higher hydrostatic pressure at the arterial end of a capillary favours the passage of protein free fluid into the precapillary space. At the venous end of the capillary where the hydrostatic pressure is lower than the osmotic pressure and lower than the extravascular tissue pressure, reabsorption takes place.

In advanced cirrhosis with portal hypertension, the vascular osmotic pressure is decreased due to associated hypoalbuminaemia and intravascular hydrostatic pressure is increased due to portal hypertension, which favours the loss of fluid into the extravascular space (peritoneal cavity).

Actually, the problem is far more complex. Although basic elements of Starling's equilibrium "portal hypertension and hypoalbuminaemia" are valid, many additional factors participate.

1. Role of portal hypertension:

Many cirrhotic patients with portal hypertension do not have ascites. Both clinical and experimental portal

vein thrombosis, which is associated with portal hypertension, rarely causes ascites (Child et al., 1952).

Many cirrhotic patients with hypoalbuminaemia have no ascites. Peripheral oedema is a far more common consequence of hypoalbuminaemia than ascites.

Hepatic venous obstruction, however, is almost always associated with ascites. If hepatic outflow obstruction is complete or nearly so, as occurs in advanced cirrhosis, tumour compression, hepatic vein thrombosis (Budd-Chiari Syndrome), the onset of ascites is rapid and often intractable. In this case ascites forms rapidly before any change in serum albumin concentration does occur.

A similar syndrome although less overt may occur in patients with severe cardiac disease such as constrictive pericarditis or advanced right-sided congestive heart failure.

When hepatic outflow obstruction predominates (post-sinusoidal obstruction), for example, if hepatic venules obstructed by regenerative nodular hypertrophy, the pressure elevation can be transmitted in retrograde fashion only to the intrahepatic sinusoidal bed. In alcoholic cirrhosis one of the major causes of increased pressure is obliteration of intrasinusoidal communication, which diminishes dissipation of pressure throughout the sinusoidal bed. The resulting increase in sinusoidal pressure is aggravated by hepatic arterial inflow, which flows directly into obstructed hepatic sinusoidal bed.

The increased sinusoidal pressure results in exudation of fluid from sinusoids into the perisinusoidal spaces. The hepatic lymph system carries as much as possible and the excessive fluid exudates from the surface of the liver into peritoneal cavity (Hyatt and Smith, 1954). Ascitic fluid which is formed, has a high protein content which can approach 4.0 gm/100 ml. Lymph leaving the liver and entering the thoracic duct is also rich in protein. The similarity of fluid in appearance and composition to hepatic lymph has led to conclusion that the fluid exudated is largely hepatic lymph (Gray, 1951).

On the other hand, if portal hypertension is caused by schistosoma ova which lodge in small portal venules (inflow or presinusoidal obstruction), the increase in pressure occurs upstream to obstruction and is transmitted back to the splanchnic vessels and spleen. Although splanchnic venous hypertension may give rise to ascites (Witte et al., 1969), it only does so occasionally and usually as end stage schistosomiasis with "pipestem" fibrosis, and ascites tends to have low albumin concentration. This is due to impermeability of portal capillaries to protein molecules despite elevated hydrostatic pressure.

Portal hypertension plays an important permissive role in ascites formation when accompanied by salt retension and/or hypoalbuminaemia. It rises capillary filtration pressure, increases the quantity of ascitic fluid and determines its localization to peritoneal cavity. Disappearance of ascites after porto-systemic shunt operation which is accompanied