SIGNIFICANCE OF IgA IN ASCITIC FLUID IN CIRRHOTIC ASCITES WITH AND WITHOUT BACTERIAL PERITONITIS

Thesis
Submitted for the Partial Fulfilment of the
Master Degree of Internal Medicine
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1991

ACKNOWLEDGEMENT

I am honoured to express my deep gratitude to **Prof. Dr. Soheir Sheir**, Professor of Internal Medicine, Ain Shams University, for her incredible encouragement, guidance and advice. She inspired the idea. Indeed without her most respectable enthusiasm, this work would have never been born. No words can express her generous guidance and wise criticism.

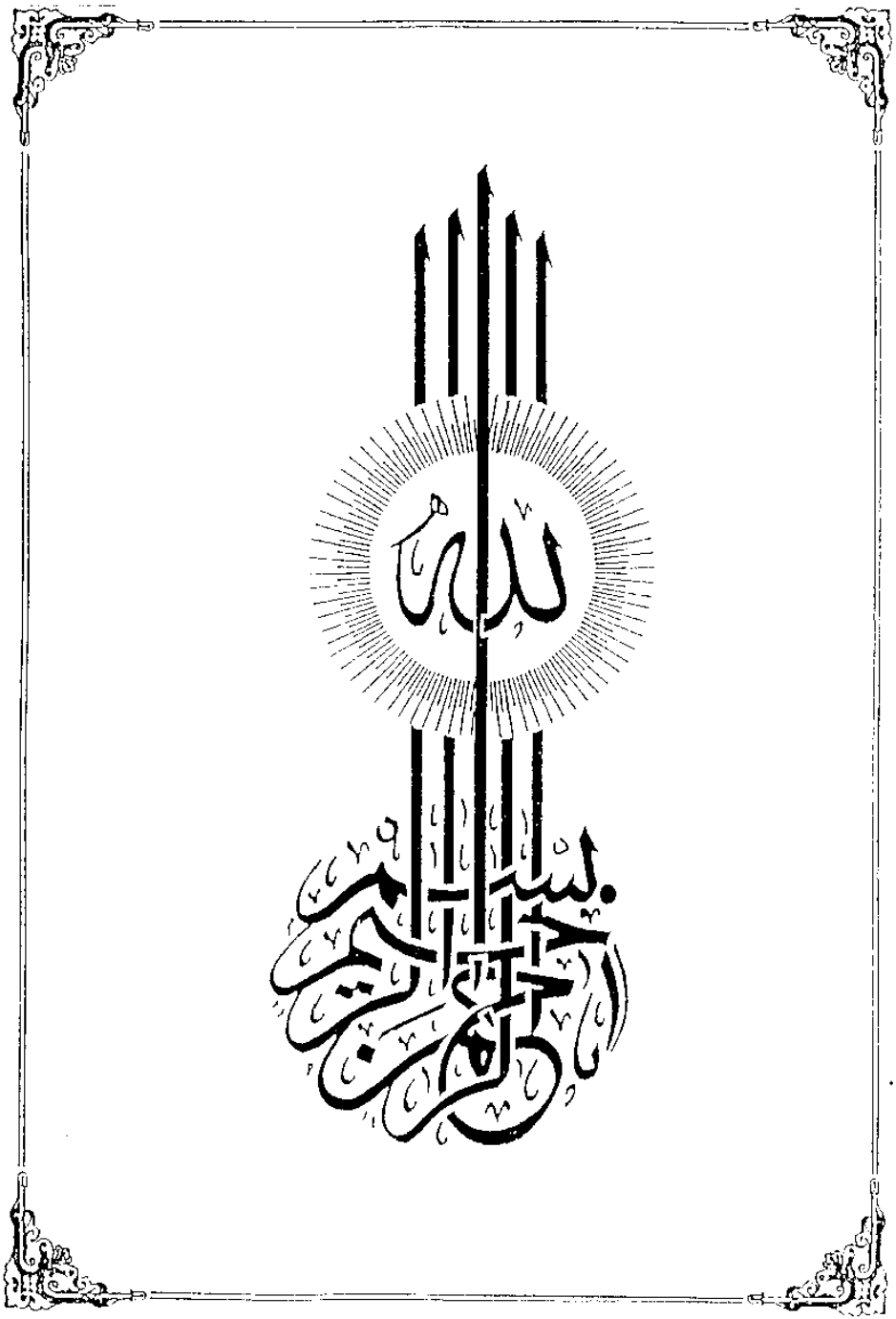
I am honoured to thank **Prof. Dr. Abla Abdel Salam Haroun**, Professor of Bacteriology, Ain Shams University, for her kind help and cooperation in the practical part of the study.

I am greatful to **Dr. Mohsen Maher**, Assistant Professor of Internal Medicine, Ain Shams University, for his valuable guidance, advice and supervision of this work.

I like to thank **Dr. Sayed Shalaby**, Lecturer of Internal Medicine, Ain Shams University, for his kind help especially during the first steps of the study.

I also like to express my deep gratitude to **Dr. Taghrid Hamed**, Lecturer of Bacteriology, Ain Shams University, for her kind help in the practical part of the study.

Last, but not least, no word can ever thanks my evergiving colleagues for their continuous help.



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INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

Ascites is a common major complication of end stage liver cirrhosis and usually carries a bad prognosis.

Spontaneous bacterial peritonitis (SBP) is often a fatal complication of cirrhotic ascites and its incidence approaches 25% of cases due to the recognition of less typical forms preceeding the full blown syndrome.

This complication may be due to direct spread of organisms through the gastrointestinal mucosa due to affected permeability of the gut wall by oedema of the splanchnic tissues because of venous and lymphatic congestion in the presence of portal hypertension. Also, bacteraemia with haematogenous spread or contamination of lymph with lymphatic spread may occur.

On the other hand, defective host defences is regarded as the most important predisposing factor for the occurence of SBP. This impaired immune response may be in the form of defective humoral defences viz: impaired opsonisation, reduced chemotaxis, deficient complement and impaired function of immunoglobulins; defective cellular activity viz: impaired monocytic function, reduced phagocytosis and decreased number of Kupffer cells; and defective ascitic fluid antimicrobial activity.

Immunoglobulin A (IgA) is present in peritoneal fluid in proportion similar to its level in serum. It activates the alternative pathway of complement, may help opsonisation, may promote antibody-dependent cell mediated cytotoxicity, may be important in antigen clearance from serum and immune regulation, and protects against mucosal infection.

AIM OF THE WORK

The aim of this work is to study serum and ascitic fluid IgA, due to its important immunological role as one of the host defensive mechanisms, to assess its role and to correlate their levels to the presence of bacterial peritonitis.

REVIEW OF LITERATURE

ASCITES

Definition:

Ascites is a collection of extracellular (free, non-purulent) fluid in the peritoneal cavity resulting from an imbalance between inflow and outflow of the peritoneal fluid through the peritoneal membrane (Reynolds and Campra, 1985).

It is not a disease but a manifestation of various organs diseases. It is a common major complication of liver cirrhosis and usually carries a bad prognosis. In normal individuals, the peritoneal cavity contains about 100- 200 ml of free non-purulent fluid.

Ascitic fluid dynamics:

Ascitic fluid is not a sequestered, static collection; there is continuous movement of fluid and solutes into and out of the peritoneal cavity (Reynolds and Campra, 1985).

Ascites is in dynamic equilibrium with the plasma, half of the amount present leaves and enters the peritoneal cavity every hour (Birkenfeld et al., 1958).

Fourty to eighty percent of ascitic water is exchanged with that of blood each hour and when the rate of fluid entering the peritoneal cavity exceeds the rate leaving it,

ascites is formed. There is also a dynamic equilibrium between ascitic fluid proteins and plasma proteins (Prentic et al., 1952).

Albumin and globulin interchange between blood and ascites but albumin turnover is more rapid (McKee et al., 1952). 4% of albumin diffuses from plasma to ascitic fluid per hour that is why intravenous albumin infusion increases the ascitic fluid albumin concentration and serum albumin rises when intraperitoneal albumin is administered (Shoeb, 1959).

Pathophysiology:

Ascites results from an imbalance of factors favoring exudation of fluid from the vascular compartment over those which maintain vascular volume.

According to Starling in 1896, the transudation of fluid between capillaries and tissue spaces is determined by the equilibrium of hydrostatic and oncotic factors in the two compartments (Sherlock, 1989).

The exchange of materials between ascites and circulation is mediated by peritoneal membrane and modified by lymphatic system.

I- Role of the peritoneal membrane:

Fluid exchange between ascitic fluid and blood occurs through the enormous capillary bed under the visceral peritoneum (Sherlock, 1989).

Peritoneal permeability is an important factor in ascites production (Mankin and Lowell. 1948). Peritoneal permeability increases in liver cirrhosis probably due to associated malnutrition that increases capillary permeability. If the patient's nutritional state and his plasma protein level are corrected, peritoneal permeability decreases and albumin no longer passes into ascitic fluid (Kark, 1951).

II- Role of the lymphatic system:

In patients with cirrhosis of the liver, the hepatic hilar lymphatics are grossly distended (Baggenstoss and Cain, 1957), and flow of lymph in the thoracic duct is greatly increased (Dumont and Mulholland, 1960) reaching 8 - 9 L/day in patients with cirrhosis and reaching about 20 L/day in patients with ascites and cirrhosis (Witte et al., 1971).

Distended and tortuous lymphatics are often seen in the liver parenchyma (Reynolds and Campra, 1985). These lymphatic abnormalities are most obvious in patients with ascites.

Inability of the lymphatic system to divert more fluid from the liver may be responsible for ascites formation (Blomstrand, 1960) and when the thoracic duct is externally cannulated, large amount of lymph is drained and ascites is promptly ameliorated (Dumont and Witte, 1966) but this is not a practical form of therapy.

In bilharzial fibrosis, there is inflow (presinusoidal) obstruction and increased hepatic lymph plays no role in ascites formation (Mousa et al., 1960) but in some cases, intestinal telangectasia and lymphatic obstruction in portal tracts of liver were detected, indicating a possible role of lymphatic obstruction which explains the occurrence of protein losing enteropathy and ascites in those patients (Elwi and Attia, 1962).

In post-sinusoidal obstruction, the sinusoidal pressure increases which results in more exudation of fluid from the sinusoids into the perisinusoidal space and formation of hepatic lymph. The lymphatic system carries as much as it can and the excessive fluid exudates from the surface of liver into the peritoneal cavity (Hyatt and Smith, 1954).

Hepatic lymph production overcomes the difficulties in interpreting the mechanism of ascites formation by Starling law of equilibrium but it neither explains the pathogenesis

of ascites in patients with extrahepatic portal obstruction nor why ascites decreases after end to side porto-caval shunt which does not releive the hepatic outflow block.

III- Role of portal hypertension:

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

The increase in pressure in the portal system causes fluid to leave the portal vasculature, primarily in the liver. Ascites develops when the rate of fluid transudation exceeds the capacity of the hepatic lymphatics and the peritoneal absorptive mechanism. Evidences point to the hepatic sinusoids as the primary site of fluid leakage rather than the mesenteric and intestinal capillaries (Reynolds and Campra, 1985).

The electron microscopic examination shows extremely porous sinusoidal wall (Numerous fenestrations of lining cells) permitting free communication with the space of Disse, bathing the microvilli of lymphatics. The normal intrasinusoidal pressure is 3 to 5 mmHg, it may rise as high as 25 mmHg in chronic liver disease and this markedly

increases fluid loss from the sinusoids and the formation of hepatic lymph (Reynolds and Campra, 1985).

When hepatic outflow obstruction (post-sinusoidal obstruction) predominantes, as in case of regenerative nodular hypertrophy which causes obstruction of hepatic venules, the high pressure is retrogradally transmitted only to the intrahepatic sinusoidal bed. Ascites is produced much easier by hepatic vein constriction than by portal vein constriction (Volwiler et al., 1950).

Constrictive pericarditis and advanced right-sided congestive heart failure cause a similar effect. Complete outflow obstruction, as in Budd-Chiari syndrome, causes rapid formation of severe intractable ascites even before serum albumin concentration decreases. Intrasinusoidal obstruction, as in alcoholic cirrhosis, is aggrevated by the direct flow of hepatic arterial blood into the obstructed hepatic sinusoidal bed. The ascitic fluid formed is of high protein content (can approach 4 gm/100 ml.) and is similar in composition and appearance to hepatic lymph which points to that the fluid exudated is largely hepatic lymph (Gray, 1951)

When inflow obstruction (Peritoneal obstruction) predominates, as in portal hypertension due to schistosoma ova lodged in small portal venules, the high pressure is

transmitted back to the splanchnic vessels and spleen. Splanchnic venous hypertension may give rise to ascites (Witte et al., 1979) usually as end stage schistosomiasis with pipestem fibrosis and after episodes of variceal bleeding when plasma oncotic pressure may be temporarily lowered.

Ascites due to portal hypertension tends to have low albumin concentration due to impermeability of the portal capillaries to protein molecules despite high hydrostatic pressure. No particular level of portal hypertension consistently produces ascites as its formation depends on the balance between speed of formation and capacity for reabsorption (Reynolds and Campra, 1985). Differences are likely among patients in:

1) The permeability of sinusoids, especially to albumin.
2) The precise location in the liver of the major increase in resistance to blood flow.
3) The size and capacity of the hepatic lymphatics.

Portal hypertension when accompanied by salt retention and/or hypoalbuminaemia has permissive role in ascites formation as it rises capillary filtration pressure (Hydrostatic pressure), increases the amount of ascites and localizes it into the peritoneal cavity (Berman and Hall, 1952). Ascites may disappear by reduction of portal venous pressure after porto-systemic shunt operation (Berman and