Prevalence of Adrenocortical Insufficiency in Patients with Liver Cirrhosis, Liver Cirrhosis and Septic Shock and in Patients with Hepatorenal Syndrome

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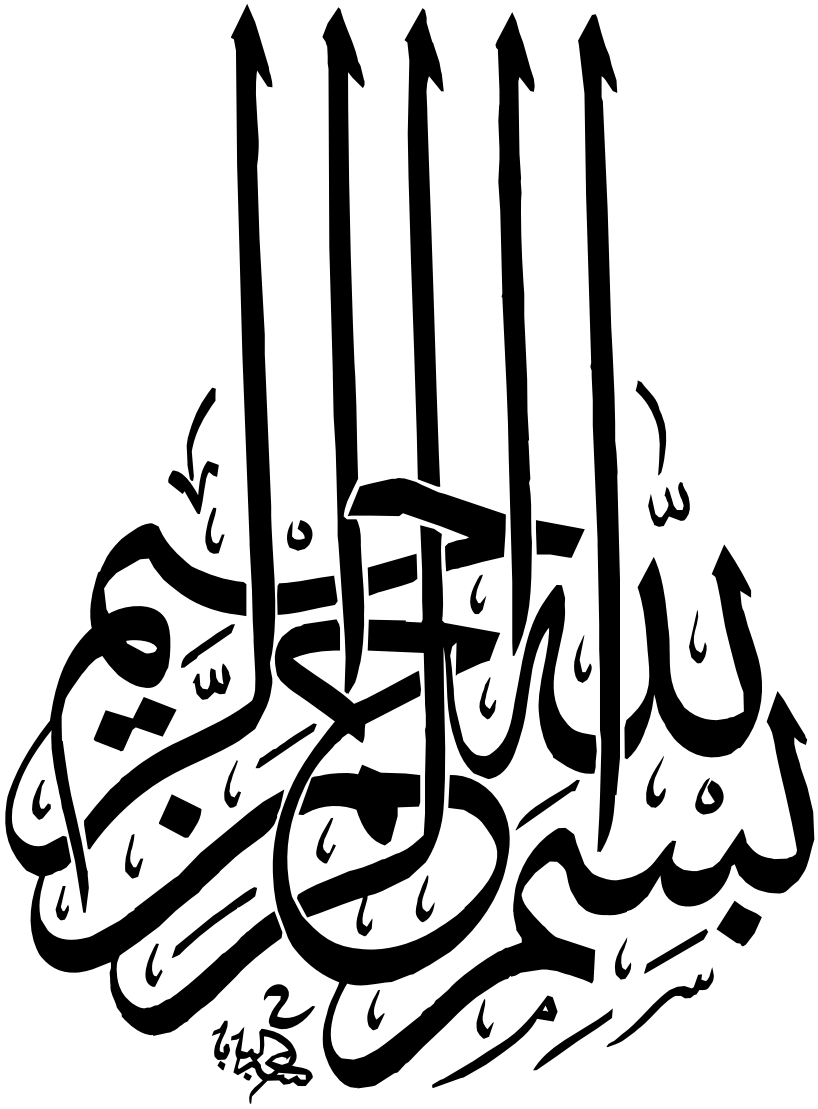
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Abstract

Background: Numerous papers have reported a high incidence of adrenal failure in critically ill patients, including those with end stage liver disease .
The term hepatoadrenal syndrome has been used to describe such an association between liver disease and adrenal failure and the definition of this term extends beyond the occurrence of sepsis, which is a frequent complication of liver failure.

Objective: to detect Prevalence of Adrenocortical Insufficiency in Patients with Liver Cirrhosis, Liver Cirrhosis and Septic Shock and in Patients with Hepatorenal Syndrome**.**

Methods: our study was conducted on three groups of patients (total 45 patients) 21 patients were males 24 patients were females With mean age 57.44± 9.95. (Cross sectional study) in whom adrenal function was assessed by synacthen test which was performed within the first 24 hours of admission. They were divided into 3 groups All included patients were subjected to full clinical evaluation , MELD scoring and child classification ,routine laboratory investigations , synacthen test was performed within the first 24 hours of admission..

Results: Our results showed that adrenocortical insufficiency was found in 33 patients from the whole 45 patients (73.3% of all patients had adrenocortical insufficiency).Patients with child C liver cirrhosis has more risk to have adrenocortical insufficiency than patients with child A ,B liver cirrhosis (P value = 0.013).Cirrhotic Patients with high MELD score have higher incidence of adrenocortical insufficiency(p=0.008). MELD score may be a good predictor for adrenocortical insufficiency With MELD cut off score 25.5 sensitivity was 0.727 and specificity was 0.750 Cirrhotic Patients with renal impairment have higher incidence of adrenocortical insufficiency :patients with high serum creatinine level have higher incidence of adrenocortical insufficiency (p=0.027), patients with high serum BUN level have higher incidence of adrenocortical insufficiency (p=0.012)

Conclusion: In conclusion, adrenal dysfunction is common in patients with cirrhosis and in patients complicated by hepatorenal syndrome. In patients with liver cirrhosis Adrenal dysfunction is associated with renal dysfunction. It occurs more frequently in patients with more severe liver disease and Correlates with disease severity scores.According to our study MELD score and serum Bilirubin level may be good predictors for hepatoadrenal syndrome.

Key words: liver cirrhosis, Child classification, hepatoadrenal syndrome, hepatorenal syndrome,. adrenocortical insufficiency ,MELD score .

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List of Abbreviations

ACCP : American Collegue Of Chest Physicians.

ACLF : Acute or Chronic Liver Failure;

ACTH : AdrenoCorticoTrophic Hormone

ALI : Acute Lung Injury

ALT : Alanine aminotransferase

ALF : Acute liver failure;

ANOVA : Vanalysis of variants

APC : Activated Protein C.

ARDS : Acute Respiratory Distress Syndrome

AST : Aspartate aminotransferase

BUN : Blood Urea Nitrogen

CBC : Complete Blood Count

CBG : Corticosteroid binding globulin

CIRCI : Critical illness-related corticosteroid insufficiency

COPD : Chronic Obstructive Pulmonary Disease

CRH : Corticotrophin releasing hormone

CVVH : Continuous veno-venous haemofiltration

DHEA : Dehydroepiandrosterone

DHEAS : Dehydroepiandrosterone sulfate

DVT : Deep vein thrombosis

ER : Endoplasmic reticulum

GFR : Glomerular filtration rate

H2 blocker: Histamine receptor 2

HRS : Hepatorenal Syndrome

ICU :Intensive Care Unit

IL : Interleukin

INR : International normalized ratio

IV : Intravenous.

LMWH : Low-molecular weight heparin

LPS : Lipopolysuccharide.

MARS **:** Molecular Adsorbents Recirculating

MAP : Mean arterial Pressure.

Mmhg : Millimeter mercury.

NAFLD : Non Alcholic Fatty Liver Disease.

NASH : Non Alcholic SteatoHepatitis.

NF-κB : Nuclear Factor κB.

NO : Nitric Oxide

OLT : Orthotopic liver transplantation

PC : Prothrombin concentration

PLA2 : Phospholipase A2

PPAR : Peroxisome proliferator-activated receptor

PT : Prothrombin time

rhAPC : Rrecombinant Activated Proteic C.

RAI **:** Relative adre nal insufficiency

RCT **:** Ranamized controled trials

RIA : Radioimmunoassay.

SBP : Systolic Blood Pressure.

SCCM : Socity of critical care medicine

SD : Standard Deviation.

SIRS : Systemic Inflammatory Response Syndrome.

SOFA : Sequential Organ Failure Assessment

TBRI : Theodor Bilharz Research Institute

TF : Tissue Factor.

TLRs :Toll Like Receptors.

UFH : Unfractionated heparin

Introduction

Critical illness is accompanied by the activation of the hypothalamic-pituitary-adrenal (HPA) axis, which is highlighted by increased serum corticotropin and cortisol levels.[1-3] The activation of the HPA axis is a crucial component of the host's adaption to severe stress.

Cortisol is essential for the normal function of the immune system, maintenance of vascular tone, and various cellular functions. In patients with severe sepsis, the integrity of the HPA axis can be impaired by a variety of mechanisms.[1,4] Recently, the concept of relative adrenal insufficiency has been used to describe a subnormal adrenal response to adrenocorticotropin in severe illness, in which the cortisol levels, even though high in terms of absolute value, are inadequate to control the inflammatory situation.[1] The short corticotropin stimulation test (SST) is most commonly used to evaluate the appropriateness of the adrenal response in this setting.

Numerous papers have reported a high incidence of adrenal failure in critically ill patients, including those with end stage liver disease and liver transplant recipients.[5]

The term hepatoadrenal syndrome has been used to describe such an association between liver disease and adrenal failure and the definition of this term extends beyond the occurrence of sepsis, which is a frequent complication of liver failure.[5]

Patients with cirrhosis share many similar hemodynamic features with patients with septic shock and adrenal insufficiency, namely, increased cardiac output, decreased peripheral vascular resistance, decreased mean arterial pressure, and hypo-responsiveness to vasopressors.[1,6]

Consistent with observations in septic patients, hemodynamic impairment is closely related to mortality and morbidity in patients with cirrhosis.[6,7,10] Studies have shown that cirrhosis in animals and humans is characterized by increased levels of endotoxin and various inflammatory cytokines, which can contribute to hemodynamic impairment1[1-13] and potentially to adrenal insufficiency as well. Furthermore, the liver is the primary site of metabolism of adrenal steroid hormone and synthesis of cholesterol, which is the major precursor of steroid.[14]

Therefore, preexisting liver dysfunction may further disturb the activation of the HPA axis during severe sepsis and septic shock. Moreover, adrenal insufficiency in severe sepsis and septic shock may aggravate hemodynamic impairment in critically ill patients with cirrhosis, leading to a poor prognosis. In fact, Harry et al.[15] recently showed adrenal insufficiency is common and may contribute to hemodynamic instability and mortality in patients with acute liver failure.

Aim of work

Considering the high prevalence of liver cirrhosis in Egyptian population and the evolving data about association between adrenocortical insufficiency and liver cirrhosis, we felt compelled to conduct this study to:

- Detect the prevalence of adrenocortical insufficiency in Patients with liver cirrhosis.
- Detect the prevalence of adrenocortical insufficiency in Patients with liver cirrhosis patients with septic shock.
- Detect the prevalence of adrenocortical insufficiency in Patients with hepatorenal syndrome.
- To find out significant predictors for hepatoadrenal syndrome .

Chapter I

Liver cirrhosis

The word "cirrhosis" derives from Greek kirrhos, meaning "tawny" (the orange-yellow color of the diseased liver). While the clinical entity was known before, it was René Laennec who gave it the name "cirrhosis" in his 1819 work in which he also describes the stethoscope [16].

Definition:

Cirrhosis of the liver is an irreversible disorder characterized by diffuse hepatic fibrosis and the conversion of normal liver architecture into abnormal nodules. It represents a sustained healing response to chronic injury from a wide variety of causes. [17]

This process distorts the normal liver architecture, interferes with blood flow through the liver and disrupts the biochemical functions of the liver. [18]

The condition often develops insidiously without giving rise to symptoms and it is thought that about 30-40% of cases are clinically latent. It may therefore be categorized on clinical grounds as:

I• Compensated cirrhosis, in which the patient is asymptomatic and the condition is discovered during biochemical screening, routine clinical examination, or abdominal surgery for another condition