1. INTRODUCTION

Fatty liver, or fatty liver disease (FLD), is characterized histologically by triglyceride accumulation within the cytoplasm of hepatocytes (Ratziu et al., 2009). FLD refers to fat accumulation in the liver exceeding 5%–10% by weight (Szczepaniak et al., 2005). Accumulation of fat may also be accompanied by a progressive inflammation of the liver, called steatohepatitis (Donnelly et al., 2005; Bedogni et al., 2007). By considering the contribution by alcohol, fatty liver may be termed as alcoholic steatosis or nonalcoholic fatty liver disease (NAFLD), and the more severe forms as alcoholic steatohepatitis (part of alcoholic liver disease) and nonalcoholic steatohepatitis (NASH) (Adams et al., 2005; Preiss and Sattar., 2008). NAFLD is the most common cause of elevated liver function tests results, after the commonly investigated causes have been excluded (Katerina Bogdanova et al., 2006). NAFLD frequently coexists with type 2 diabetes mellitus (T2DM) because the conditions have common risk factors (Malnick et al., 2003).

NAFLD represents a spectrum of disease ranging from hepatocellular steatosis through steatohepatitis to fibrosis and irreversible cirrhosis. The prevalence of NAFLD has risen rapidly in parallel with the dramatic rise in obesity and diabetes (Charlton., 2004; Vuppalanchi., 2009).

NASH is a form of metabolic liver disease in which, steatosis is associated with lobular inflammation, hepatocyte injury and/or hepatic fibrosis (Ludwig et al., 1980; Ahmed and Byrne., 2005). NASH typically
causes no symptoms. When present, clinical features such as fatigue, hepatomegaly and aching hepatic discomfort and most of them are non-specific (Liou and Kowdley., 2006). In 20–25% of cases, NASH may progress to advanced stages of hepatic fibrosis, cirrhosis and liver failure then becomes the most common cause of death (Propst et al., 1995; Bugianesi et al., 2002; McCullough., 2005; Heidelbaugh and Bruderly., 2006; Farrell et al., 2006; Pascale et al., 2010). Occasionally, hepatocellular carcinoma (HCC) may also occur. Correction of insulin resistance by dietary measures and increased physical activity is a logical approach to prevent or reverse NASH, and modest weight reduction can normalize liver test abnormalities (Preiss and Sattar., 2008).

1.1. IMPORTANCE OF PROPER DIAGNOSIS OF NASH

NASH is an asymptomatic disease and the person with NASH will feel that he is absolutely fine and doing well. But if it is not diagnosed properly, it may lead to the cirrhosis, an end stage liver disease and there by leads to the death of the individual. The following are various factors that emphasize the importance of the proper diagnosis of NASH.

- High prevalence of fatty liver disorders in urbanized communities
- NASH now rivals alcoholic liver disease and chronic hepatitis C
- NASH is a potential cause of cirrhosis, which may be ‘cryptogenic’, and lead to end-stage liver disease
- Liver failure is most common cause of death in patients with cirrhosis resulting from NASH
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- Standardised mortality of liver disease in type 2 diabetes greatly exceeds vascular disease
- Role of metabolic determinants of NASH in pathogenesis of other liver diseases, particularly hepatitis C and alcoholic cirrhosis

1.2. METABOLIC CONDITIONS ASSOCIATED WITH NASH

Although the cause of NASH is unknown, it is most frequently seen in people with one or more of the following conditions (Byrne et al., 2009):

- Type 2 diabetes mellitus
- Insulin resistance
- Obesity
- Hyper triglyceridaemia

Although the pathogenesis of NAFLD / NASH is not yet fully understood, much progress has been made in recent years in elucidating the mechanisms of progression from steatosis to more advanced liver inflammation and fibrosis. With this objective in mind, an attempt has been made to discuss the current understanding of NASH pathogenesis, and anticipate that such knowledge will eventually translate into the development of novel treatment strategies.

Human and animal studies have started to address key issues in NASH pathogenesis, such as the nature of insulin resistance and why it occurs, whether it is responsible for inflammation or liver cell injury as well as free fatty acid accumulation, the mechanisms for inflammatory recruitment and perpetuation, the biochemical basis and significance of
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oxidative stress and the pathogenesis of fibrosis (Edmison and McCullough., 2007; London and George., 2007).

The present study is concerned with exploring the potential effects of pioglitazone, quercetin and hydroxy citric acid in experimental model of Non Alcoholic Steatohepatitis (NASH) by assaying various biochemical parameters and histopathological manifestations.