



Diabetes mellitus and fatty liver disease: Which comes first?

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The diabetes mellitus as a important part of metabolic syndrome is an emerging disease and association with fatty liver is very common. Reading this editorial is recommended to all family physicians, internists, gastroenterologists, endocrinologists and health policy makers.

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Metabolic syndrome is an emerging problem in the world (1). Diabetes mellitus is one of the main parts of metabolic syndrome, and insulin resistance, hypertension, low HDL cholesterol, and hypertriglyceridemia are other parts of this syndrome (2). There is a worldwide epidemic of diabetes and obesity, with an estimated one billion overweight adults (3). It has been reported that the prevalence of metabolic syndrome in Iran is one of the highest worldwide (1). Metabolic syndrome is the disease that has changed the scientific knowledge in the new millennium. Nonviral diseases such as coronary heart disease and cerebrovascular accident were major global pandemics at the start of the 21st century. As risk factors for these diseases, physicians gave more attention to diabetes, hypertension, hyperlipidemia, and obesity. But now a new epidemic is emerging, metabolic syndrome, which is a cause of all risk factors for cardiovascular and cerebrovascular problems. As its name suggests, it is a syndrome i.e., a series of presentations that collectively form a categorization of pathophysiology, so metabolic

syndrome is still forming and changing.

Fatty liver disease has been diagnosed as an incidental finding in abdominal ultrasonography with a diffuse increase in echo texture (bright liver), increased liver echo texture compared with the kidneys, vascular blurring, and deep attenuation (4). Fatty liver disease can be found in patients with diabetes mellitus and obesity or can be diagnosed in individuals without these diseases. This raises questions regarding the influence of fatty liver disease on mortality and the risk of diabetes in the future (5). The spectrum of disorders related to obesity is wide, but the most important are insulin resistance, type 2 diabetes mellitus, abnormality in lipid profiles, high blood pressure, cardiovascular disease, stroke (6), and fatty liver disease (7, 8). Fatty liver disease in its more progressed phase, nonalcoholic steatohepatitis (NASH), is a component of metabolic syndrome and its consequences, and it is not surprising that elevations in ALT activity are frequently present in people with diabetes mellitus and cardiovascular disease and are associated with increased mortality (9). Liver-function tests are the most frequently ordered tests in clinical practice, being relatively cheap and easy to measure. ALT is the most common screening test for necro-inflammation in the liver, but it can be abnormal in the presence of inflammation and if most

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of the low-grade fatty liver is in the normal range. Elevations in ALT activity usually reflect the presence of fatty liver and are associated with obesity, cardiovascular disease, cerebrovascular disease, hypertension, and mortality. An abnormal ALT level should be viewed as an indicator of metabolic syndrome and should be addressed quickly. These patients are more likely to die of cardiovascular disease than from liver disease (4). Markers of insulin resistance are impaired glucose metabolism, hypertriglyceridemia, and fatty liver. The liver is a main site of glucose reuptake and also glycogenolysis. So, changing the responsiveness of liver to insulin effects (i.e., hepatic insulin resistance will disturb the whole body metabolism of glucose). On the other hand, when the process of insulin resistance and metabolic syndrome begins, it may cause increased fat deposits in the body and liver of animals. The abnormal ALT can predict for occurrence of diabetes mellitus in future.

Furthermore, metabolic syndrome and insulin resistance are more common in patients infected with hepatitis C virus (HCV) and hepatitis B virus (HBV), and the prevalence is increasing today (10). The degree of fibrosis is higher in these patients with coincidental diabetes mellitus and fatty liver disease (11, 12). There is a wide range in the prevalence of glucose metabolism alterations in cirrhotic patients in various studies (12, 13). The frequency of diabetes mellitus increases significantly with the severity of the liver disease both in cirrhotic cases and in patients with chronic hepatitis. These findings suggest that liver fibrosis, but not cirrhosis itself, is the event associated with glucose intolerance (12). But the multivariate analysis indicates an independent association between chronic hepatitis and DM rate, despite the fact that we compared diabetes mellitus occurrence among three groups who all suffered from liver disease. This theory states that occurrence of insulin resistance initially facilitates lipolysis and increases free fatty acid deposition in the liver, which increases products of lipid peroxidation inducing oxidative stress. This results in cytokine-mediated hepatic inflammatory damage that induces collagen deposits and eventually fibrosis.

In conclusion, a high prevalence of diabetes mellitus in patients with fatty and nonfatty liver share a common pathophysiology, and doctors should alert their patients that fatty liver puts them at high risk of acquiring diabetes mellitus and cardiovascular disease in the future. In fact, the risk of diabetes mellitus, its complications, and

cardiovascular disease are more important than the progression of fatty liver to end-stage liver disease. Unfortunately, most affected persons are asymptomatic, and they are unaware of their endocrine abnormality. This finding highlights the importance of periodic screenings of individuals at high risk for metabolic syndrome.

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