HEPATIC DYSFUNCTION IN DIABETES

Dr. Vivek Chandra¹

As we know that Diabetes Mellitus is a disorder of impairment of carbohydrate metabolism and thus has varied systemic consequences. This review is an attempt to bring out any possible associations between Diabetes Mellitus and the liver. The metabolic dysregulation associated with Diabetes Mellitus causes secondary changes in multiple organ systems that impose a tremendous burden on the patient and the health care system.(1)

The process of glycogenesis builds up glycogen stores in the liver by utilizing glucose derived by carbohydrate metabolism. The liver plays a vital role in maintaining steady blood glucose levels either by gluconeogenesis or by glycogenolysis. Glucose in blood is taken up by body tissues to maintain their normal functioning. In the cell, the glucose moiety is converted to glucose-6-phosphate which subsequently undergoes glycolysis. A deficiency of substrate for gluconeogenesis because of muscle wasting in patients with impaired hepatocellular function or decreased hepatic blood flow may cause hypoglycemia.(2)

Often Liver diseases lead to diabetes and vice versa. Diabetes Mellitus makes patients more prone to liver diseases but at times the occurrence coincides. The presence of insulin in the blood stimulates glycogen synthesis in the liver. Apparently, reduced glycogen synthase activity may be associated with insulin-deficient states but some studies have shown presence of excess glycogen deposits in the liver.(3,4) Clinically symptoms such as hepatomegaly have shown regression by use of insulin injections(3).

Progression of early liver disease to liver fibrosis and liver cirrhosis may occur due to insulin resistance.(5) Serum resistin appears to be a useful biomarker in patients with chronic liver disease and may be involved in the pathogenesis of insulin resistance in the liver.(5)

Diabetes Mellitus type 2 and Diabetes Mellitus type 1 (poorly controlled) show association with fatty liver and increase in fat content of the liver.(3,4)

¹MBBS, Clinical MD Fellow, WLPMS-Ealing Hospital NHS Trust, Uxbridge Road, Middlesex, UK
These fatty changes are picked up by USG but the early microscopic changes of onset are missed. A routine liver biopsy in all diabetics with hepatomegaly, till date, encourages debate.

Other causes for a fatty liver may be obesity, alcoholic liver disease, hepatotoxins e.g. carbon tetrachloride etc., Wilson’s disease and drugs such as tamoxifen, esterogen etc.

As an effect of diabetes on adipocytes and liver, a differential regulation of phosphotyrosine phosphatase (PTPase) and phosphoserine phosphatase (PSPase) has been noted and studies indicate lower galactosyltransferase activity in diabetic livers. (6,7)

Maternal diabetes effects fetal liver cells and chronic uncontrolled hyperglycemia can alter chromatin structure in vivo. Some findings suggest a model of multiple susceptibility genes expressed both in liver and pancreas. (8,9)

As far as liver cirrhosis is concerned, it is unlikely that Diabetes Mellitus predisposes to cirrhosis but confounding factors like obesity, fatty liver, hepatitis etc may have a role in the high frequency of cirrhosis seen in diabetic patients. Cirrhotic patients may show normal or low HbA1c levels despite altered glucose metabolism, making the test not reliable. The incidence of cirrhosis in diabetics has been found to have a wide range from 0.4 percent (Joslin and colleagues) to as high as 30 percent in other studies. (10) The association of genotype 2a of hepatitis C virus with diabetes makes the relationship interesting. (11) Some scientists suggest pancreatic beta cells as an extrahepatic target of HCV (12). Evidence suggest that chronic hepatitis C is associated with increased risk of development of type 2 diabetes, irrespective of presence of cirrhosis. (13)

Post orthotopic liver transplant patients are predisposed to developing diabetes. (14). The immunosuppressants like FK506 and cyclosporine along with heavy doses of steroids might predispose transplant patients to develop diabetes. Haemochromatosis leading to intra-organ iron deposition is commonly associated with both liver and pancreatic abnormalities, where liver abnormalities are much more common in non-insulin dependent diabetes compared to well controlled type 1 diabetes (15). Patients with autoimmune polyglandular syndrome (PAS) with components like IDDM, hypogonadism and Hashimoto’s thyroiditis also present with primary biliary cirrhosis (16).

REFERENCES:

(7) Mulay S, and Congote LF. Influence of maternal diabetes in rats on hemoglobin synthesis and uridine uptake by fetal liver cells. Diabetes 34:212-216
(8) Hartnell JM, Storrie MC and Mooradian AD. Diabetes-related changes in chromatin structure of brain, liver, and intestinal epithelium. Diabetes 39:348-353
(10) George P. Kozak, Clinical Diabetes Mellitus: 398/32
(16) Padmanabhan M, Mohan V. Diabetes and liver, MDRF: 2000