Histopathological Changes on The Kidney and Lung of Experimentally Induced Diabetic Rats

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Abstract

Background: Diabetes mellitus is an endocrine disorder characterized by a state of hyperglycemia. It is caused by defect in the insulin secretion, insulin action or even both. Long-term complications of diabetes are many as nephropathy, retinopathy and neuropathy. Diabetes mellitus is considered the most common cause of renal failure worldwide. Diabetes results in many histological changes in the kidney. Most cell types of the kidney as podocytes, tubular cells and mesangial cells affect in diabetes. The most characteristic change in diabetic nephropathy (DN) is glomerular alteration as glomerular expansion and thickened glomerular basement membrane. Many alterations of the respiratory functions are detected in diabetic patients. Several characteristic histological changes had been described in the lung of diabetic animals. Diabetic lung is characterized with increased connective tissue at the expense of alveolar air spaces. This review focuses on histological changes on the kidney and lung of diabetic animal model.

Conclusion : Kidney and lung are target organs for diabetes. DN is one of common chronic complications of diabetes. DN is the most common indication for renal replacement therapy worldwide. Several histopathological changes were reported in lung of diabetic animals. It is essential to provide novel therapeutic strategies that could prevent complication of diabetes on kidney and lung.

Keywords: Diabetes; Diabetic nephropathy; Lung .

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Introduction

Diabetes Mellitus (DM) is a metabolic disorder of chronic hyperglycemia. Diabetes is classified as immune-mediated (diabetes Type 1) or insulin resistance (diabetes Type 2) **(Cameron and Bennett 2009)**. Streptozotocin or alloxan had been used for induction of diabetes in rats. They produce diabetes by causing a selective necrosis of the pancreatic beta cells **(Tolouian and Hernandez 2013).** Complications of diabetes could be acute or chronic. Acute complications are as hypoglycemia, hyperglycemic crises and ketoacidosis. Chronic complications are as nephropathy, retinopathy , autonomic neuropathy, foot ulcer and impaired growth and development **(Ozougwu, Obimba et al. 2013).**

- **Diabetic nephropathy (DN)**

Diabetes mellitus is considered the most common cause of renal failure worldwide. Diabetes causes many changes in the renal tissue **(Ozougwu, Obimba et al. 2013).** The most important lesions in DN are the glumerular alterations **(Pourghasem et al. 2015).** Diabetic nephropathy is a serious kidney-related complication of type 1 diabetes and type 2 diabetes. It is also called diabetic kidney disease. About 25% of people with diabetes eventually develop kidney disease. Diabetic nephropathy affects kidneys' ability to remove waste products and extra fluid from the body **(Thijs et al. 2010).**

The most characteristic changes of diabetic nephropathy in experimental animals are glomerular mesangial expansion, tubulointerstitial fibrosis and thickening of basement membrane in glomeruli and tubules (**Fig.1**). These changes are caused by excessive deposition of extracellular matrix in the kidney. The increased accumulation of extracellular matrix components could be attributed to an increase in gene expression and protein synthesis such as collagen IV, laminin, and fibronectin **(Pourghasem et al. 2015).**

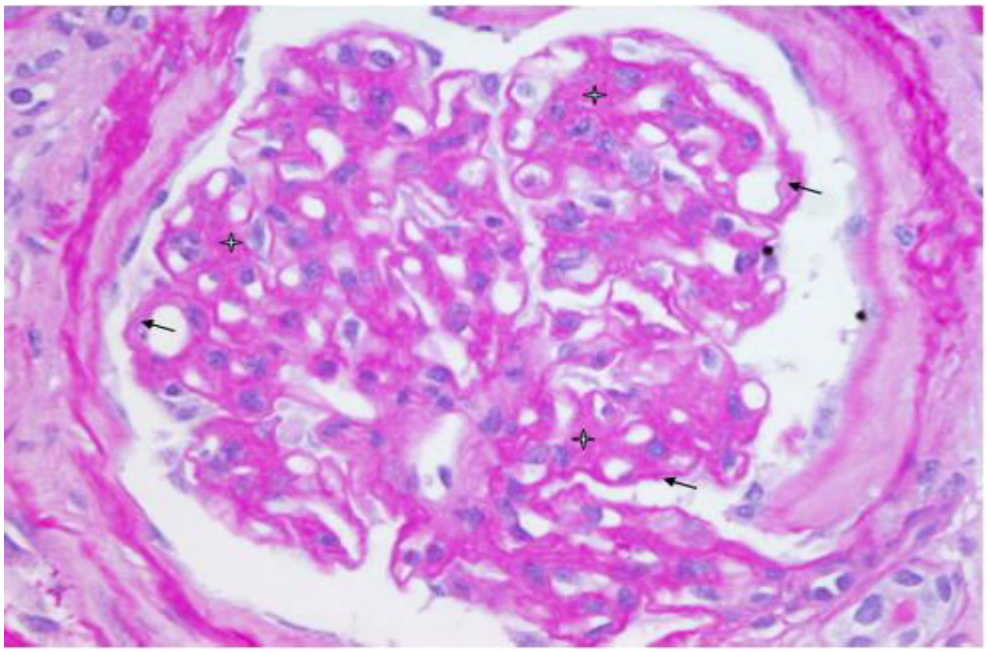

Fig.1. A Photomicrograph of a section of the kidney in diabetic nephropathy in type 1 diabetes showing diffuse expansion of mesangium (star) and diffuse thickening of the glomerular basement membrane (arrow). (PASx400) **(Đorđević and Rački 2012)**.

Diabetic nephropathy affects most cell types of the kidney as podocytes , mesangial cells, tubular cells and interstitial cells. The Renal Pathology Society classified diabetic nephropathy into four glomerular lesions (**Fig.2**). as follows: class I: thickening of glomerular basement membrane; class IIa: mesangial expansion is mild; class IIb: mesangial expansion is sever ; class III: nodular sclerosis and class IV: global glomerulosclerosis occurs in more than 50% of the glomeruli **(Zajjari et al. 2019).**

The early histological alterations in the diabetic kidney of experimental animals are tubular hypertrophy, thickening of the tubular basement membrane and interstitial inflammation with mononuclear cell infiltration **(Zajjari et al. 2019).** Studies reported degenerative changes of renal tubules as vacuolation of renal cells. It is associated with glycogen deposition or subnuclear lipid vacuolation. **(Gorboulev et al. 2012).**

In diabetic nephropathy of experimental animals, the renal arterial thickness occurred in efferent and afferent arterioles but the efferent arterioles are more affected. The renal arterial thickness is a progressive complication that could lead to hypertension and ischemic nephropathy **(Pourghasem et al. 2015).**

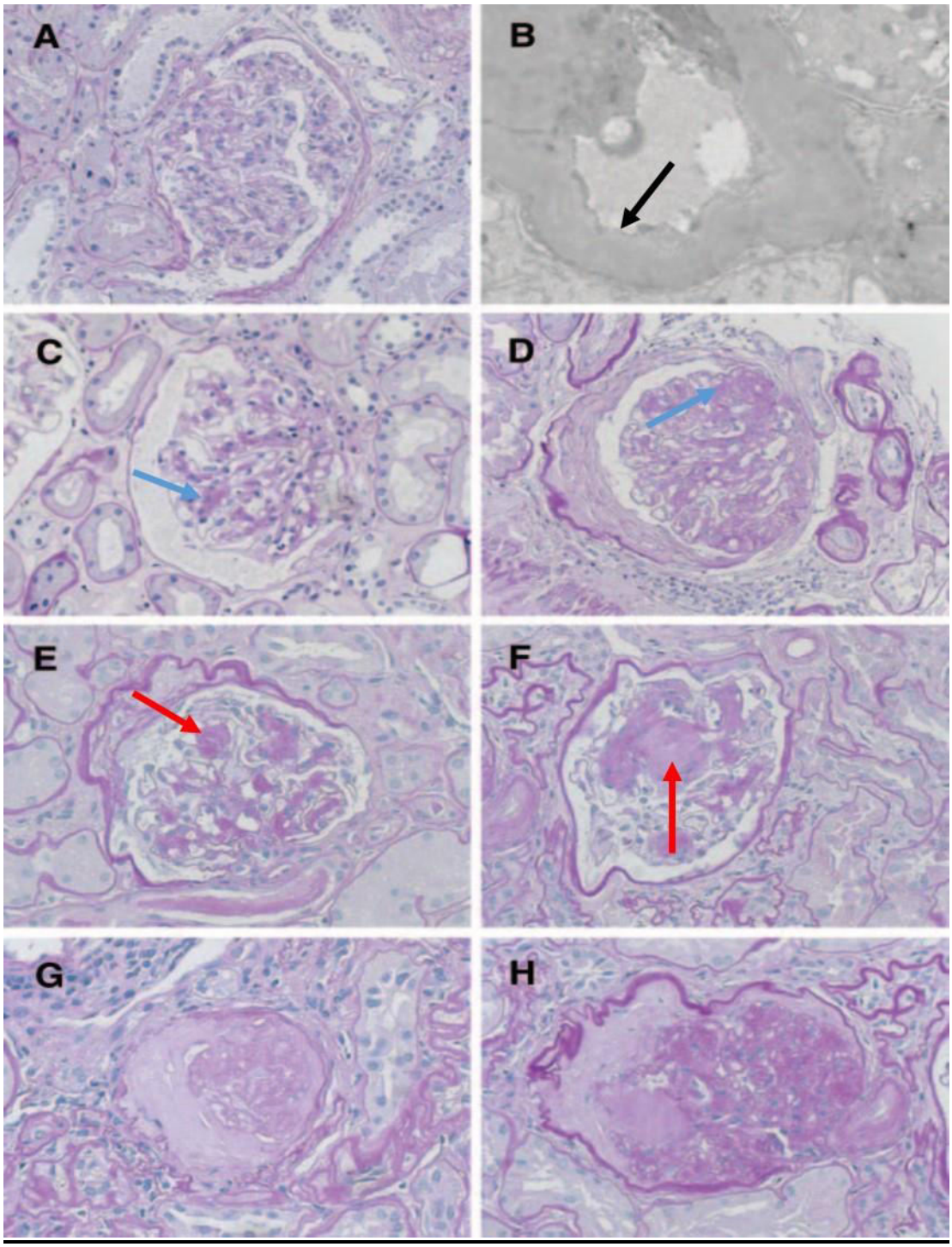

Fig.2 Representative examples of the morphologic lesions in DN. Class I (A,B) in (A) glomerulus showing only mild ischemic changes . (B) EM of this glomerulus showing mild thickening of glomerular basement membrane (arrow). Class IIa, IIb (C, D) glomeruli with mild and moderate mesangial expansion (arrow), respectively. Class III(E, F) showing nodular sclerosis (arrow). Class IV (G,H) showing global glomerulosclerosis in more than 50% of glomeruli **(Thijs et al.2010).**

- **Diabetes and respiratory system**

Diabetic patients could have many abnormalities of the respiratory function. These abnormalities are as changes of pulmonary diffusing capacity, lung volume, control of ventilation, and neuroadrenergic innervation. The studies reported many histological changes of lung in diabetic animals. They could explain these abnormalities of respiratory functions **(Komatsu et al. 2010).** The lung has great microvascular reserve. The loss of microvascular reserve in the lung may ocurr with the increased risk of hypoxia as in acute or chronic pathological lung conditions like pneumonia , asthma or chronic obstructive pulmonary disease. Studies on diabetic animals showed hyperemia of blood vessels and thickened walls **(Talakatta et al. 2018).**

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The most characteristic feature in lung of diabetic animals is collagen accumulation in lung connective tissue. The nonenzymatic glycosylation of proteins in the lungs and chest wall makes the collagen less susceptible to proteolysis and leaded to its accumulation. This process is caused by hyperglycemia. Collagen accumulation increases stiffness and rigidity of lung parenchyma and chest wall **(Bowden et al. 2010).**

Studies on diabetic animals showed thickened interalveolar septa . This thickness is attributed to increased extracellular matrix and cellular infiltration (**Fig.3**). Therefore, the air spaces decrease in size **(Pitocco, et al. 2012)**

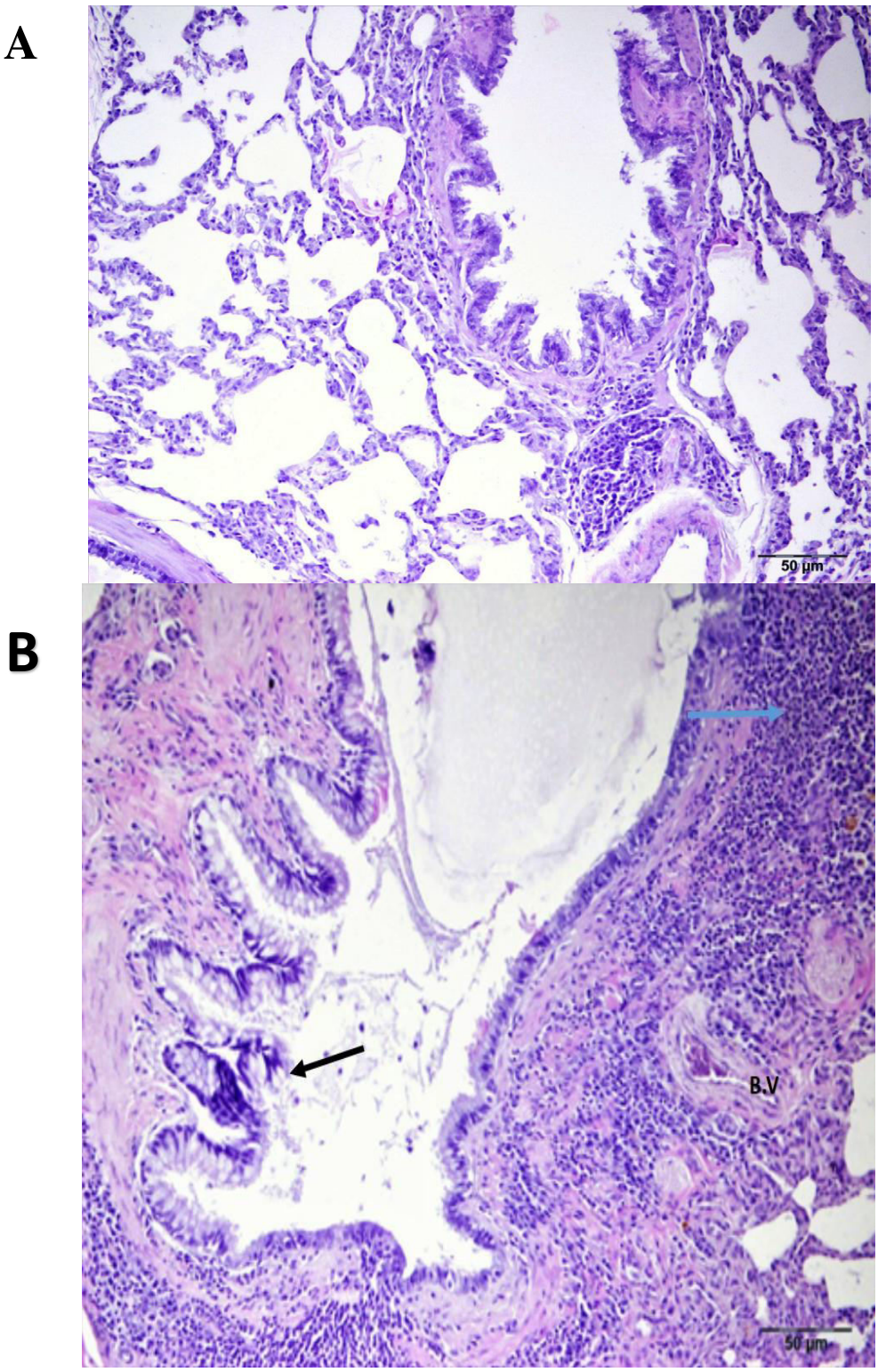

Fig.3. A Photomicrograph of a section of the lung stained with (H&E) in (A) control , (B) type 1 diabetic rats showing thickened intralveolar septum with peribronchial cell infiltration (blue arrow), desquamation of bronchiol epithelium (black arrow) and hyperemia in blood vessels (B.V) **(Onk et al. 2018).**

Abnormalities of respiratory functions could be attributed to decreased muscle strength that is caused by insulin-resistance. Myopathic and neuropathic changes of respiratory muscles affect the ventilatory pump of lung **(Pitocco et al. 2012).**

Conclusion

Diabetes can harm the kidney and the lungs. One of the common long-term consequences of diabetes is DN. The most typical reason for receiving renal replacement therapy is DN. Many histological alterations in the lungs of diabetic animals have been documented. New therapeutic approaches are critical to preventing complications from diabetes on the kidney and lung.

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