

Pathology of Diabetic Induced Neuropathy

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Diabetes and its related intricacies force huge impact on social insurance & health care network. The overwhelming inconveniences of diabetes are for macro and micro vascular disease. Micro vascular disease condition, including nephropathy, builds up a few years after the beginning of diabetes (Cade, 2008). Introduction of tissues to the high blood glucose condition called hyperglycemia, is the primary starting element of onset of diabetes neuropathy, although genetic makeup is also important in deciding the susceptibility to diabetic nephropathy. Diabetic nephropathy is the number one reason for the end-stage renal/kidney disease (ESRD) and is related to enhance cardiovascular mortality. The major symptoms of diabetic nephropathy are the continues presence of albumin in the urine along with diabetes type 1 and type 2 (Gariani et al., 2012).

The cost of treatment and care for the diabetic patient is huge in the ESRD. World health organization Renal data system incontestable a dramatic increase within the incidence of ESRD due to diabetes (Wang and Sarah, 2006). More than 44% of new cases of ESRD has been reported for diabetes patient. 40% population has been reported for diabetes between 1984-1996, but the population started treatment for ESRD has been increased to 400 times. Diabetic nephropathy occurrence in population grew to 37% between 1996-2005 and is expected to increase in further years. Afkarian et al. (2016) reported that every 4th diabetic patient in the United States of America is suffering from renal disease.

Pathological effects of diabetic nephropathy

The presence of increased albumin level in urine in diabetic nephropathy is considered to be the glomerular problem. Albumin needs to cross the glomerular barrier to excrete in urine. Loss of anionic charge means the loss of normal heparin sulphate proteoglycan which is considered to be the main glycosaminoglycan component of basement membranes of glomeruli (Wu *et al.*, 1987).

Albumin buildup in the proximal tubular cells of kidney resulted in the inflammation causing tubulointerstitial lesions (Gilbert and Cooper, 1999) and podocytes have been reported to be involved in increasing proteinuria and resulting hardening of glomeruli called

glomerulosclerosis. The negatively charged molecules enclosed the podocytes that assist in repulsion of negatively charged proteins like albumin protein. The slit diaphragm is vital to avoid proteinuria and remain open by the negative charge of podocytes. Anomalous morphology of podocytes has been reported in humans suffering from diabetes (Su *et al.*, 2010).

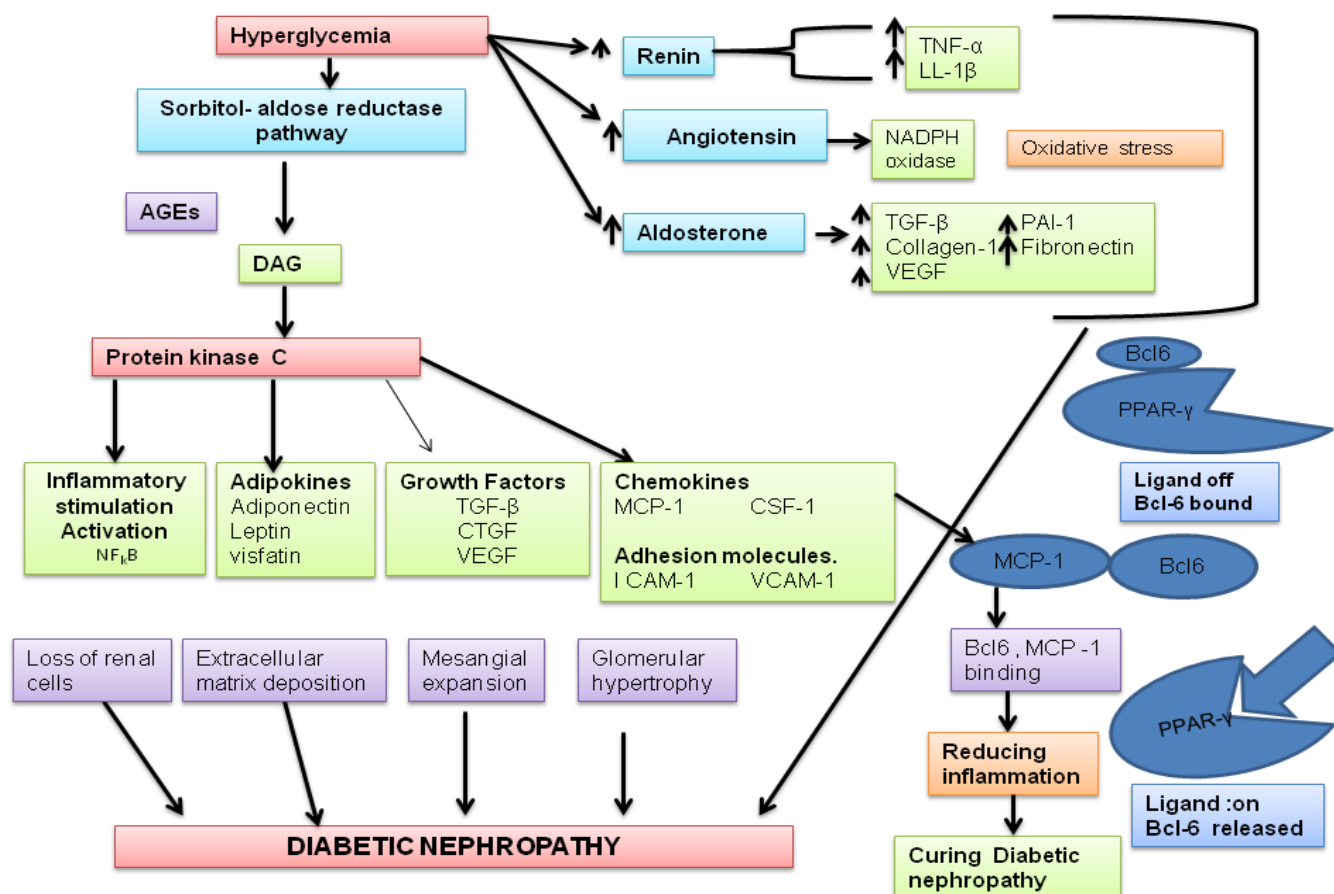


Figure1: Mechanism of Diabetic Nephropathy (Reidy *et al.*, 2014)

As suggested earlier, although genetic makeup is also important in deciding the susceptibility to diabetic nephropathy but hyperglycemia condition is the initiating factor of the disease. A number of mechanisms have been subsists for high blood glucose level that ultimately resulted to development of diabetic nephropathy. In addition to the hyperglycemic condition, certain metabolic pathway leading to diabetic nephropathy has been suggested (Table 1)

Factors	Pathway
Growth Factor and Cytokines	<ul style="list-style-type: none"> • Transforming Growth Factor β (TGF- β) • Platelet – Derived Growth Factor (PDGF) • Connective Tissue Growth Factor (CTGF) • Growth Hormone (GH) and Insulin like Growth Factors (IGFs) • Vascular Endothelial Growth factor (VEGF)
Hemodynamic Factors	<ul style="list-style-type: none"> • Angiotensin II (Ang II) • Endothelin (ET)
Metabolic Factors	<ul style="list-style-type: none"> • Advanced Glycation End Products (AGEs) • Aldose Reductase (AR) / Polyol Pathway
Intracellular Factors	<ul style="list-style-type: none"> • Diacylglycerol (DAG) – Protein Kinase C(PKC) Pathway

Conclusion

In the last few years, we have witnessed enormous progress in the understanding of the risk factors and mechanisms of diabetic nephropathy, the stages of renal involvement in diabetes, and the treatment strategies to prevent or interrupt the progression of diabetic nephropathy. However, diabetic nephropathy, still, remain a huge clinical problem despite implementation of overall intensified glycemic and antihypertensive control in these patients. Extensive research during recent years has identified several new pathways with impact on the development of diabetic kidney disease.

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