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Diabetic Nephropathy, Pathophysiology, Stages and Diagnosis: A Review Study

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ABSTRACT

Diabetic nephropathy was defined as raised protein elimination in urine. The initial stage is characterized by a limited elevation in urinary albumin elimination, also named incipient DN or microalbuminuria. Higher progressive diseases are characterized by the incidence of proteinuria or macroalbuminuria. The recent is typically called overt DN. Diabetic nephropathy, also called diabetic kidney disease, is one of the most prevalent microvascular diseases of the kidneys that results from type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus. Therefore, early disease detection is critical, as DN is the leading cause of renal disease in its latter stages and is associated with an increased risk of death in general, primarily due to cardiovascular disease.

Keywords: Diabetic Nephropathy (DN), Proteinuria, Chronic Kidney Disease.

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INTRODUCTION

Diabetic Nephropathy

Diabetic nephropathy, also termed chronic kidney disease (CKD) due to diabetes or diabetic nephropathy (Persson and Rossing, 2018), One of the most severe microvascular complications of diabetes. It is described by raised excretion rate of urinary albumin, elevated blood pressure, and failure in renal function primary to final stage of renal disorder (Mahfouz *et al.*, 2016). Diabetic nephropathy affects about one third of persons with type 1 or 2 DM (Reutens, 2014). The reported final stage renal disease (ESRD) prevalence in the Middle East ranges from 52 per million population (pmp) in Iraq to 818 pmp in Lebanon, with a mean prevalence of 430 pmp in the entire Middle East (Malekmakan *et al*, 2018).

Pathophysiology of Diabetic Nephropathy

The pathophysiology leading to an increase in DN and subsequent end-stage kidney disease stems from DM, which causes the production and movement of progressive hemodynamic, glycation end products, growth factors elaboration, and hormonal changes. These variations lead to the production of inflammatory mediators and reactive oxygen types, these variations cause glomerular hyper-filtration, renal hypertrophy, glomerular hypertension, followed by altered glomerular structure that is medically showed as albuminuria and hypertension (Umanath and

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Lewis, 2018). Psychologically, the kidneys suffer numerous alterations, comprising glomerular basement membrane thickening, extracellular matrix is removed (primarily the mesangial), proliferative alterations, and tubular atrophy, eventually causing interstitial fibrosis and glomerulosclerosis.

With the beginning of diabetes mellitus, the average increase in kidney weight and size is 15%, and this capacity rise remains even afterward advanced declines in kidney function occur. Examination of the kidney tissue reveals thickening of the glomerular basement membrane and mesangial growth. Wilson and Kimmelstiel first described the nodular pathological lesion of DN in 1936.

The nodule is typically acellular and positive for periodic acid-Schiff stain. While these nodules are pathognomonic for DN, they were found in only 10% to 50% of biopsy samples from subjects with types 1 and 2 DM (Umanath and Lewis, 2018).

Stages of Diabetic Nephropathy

DN development involves five stages:

Stage 1*:* hypertrophic hyperfiltration, in this phase, either the GFR is increased or normal. Phase 1 lasts approximately 5 years from the beginning of the condition. The capacity of the kidney is enlarged by around 20%, and renal plasma movement is elevated by 10%-15%, but blood pressure and albuminuria persist within the normal ranges (Vujicic *et al.,* 2012).

Stage 2, the quiet stage: This phase (discreet phase) classically lasts for 5-15 years after the identification of diabetes. The characteristics of the 2 phase GFR remain raised due to hyperfiltration, and Kidneys remain hypertrophied, and urinary albumin excretion (UAE) rate stays normal (Nazar, 2014).

Stage 3, the microalbuminuria phase: includes the first clinically recognized symptoms of glomerular destruction and microalbuminuria (albumin 30-300 mg/day). It typically occurs 5 to 10 years after the disease's onset, whether with or without hypertension. About 40% of subjects reach this stage (Gheith *et al.,* 2016).

Stage 4, chronic kidney failure (CKF) phase: It is the phase of CKD with permanent protein in the urine (> 300 mg/day), declined GFR under 60 ml/min/1.73 m2, and continued hypertension (Gheith *et al.,* 2016).

Stage 5, terminal kidney failure (TKF): (GFR < 15ml/min/1.73 m2), around 50% of the subjects with terminal kidney failure need kidney replacement treatment (hemodialysis, kidney transplantation, and peritoneal dialysis). In this phase, enlarged kidney capacity and altered Doppler markers may be the primary morphological symptoms of renal destruction, but GFR and proteinuria are the finest markers of the grade of destruction (Vujicic *et al.*, 2012).

Diagnosis of Diabetic Nephropathy

Proteinuria is an early and distinctive changes caused by DN. Since albumin is frequently found in chronic kidney disease (CKD) specimens, it is recommended as a protein screening modality because it can be subject to glomerular penetrability and analysis calibration (Kowalski *et al.*, 2014)

Glomerular Filtration Rate (GFR) is one of the best-used indicators for diabetic nephropathy monitoring and diagnosis and should be estimated for all patients with diabetes mellitus. Albuminuria and glomerular filtration rate might be mostly independent of each other, and glomerular filtration rate or albumin detection is inadequate to completely rise the present condition of diabetic nephropathy (Radbill *et al,* 2008).

Albuminuria

Albumin is created from the liver (MW 65 KD). The circulating life span is 12 reserve, and it is not catabolized by hunger. A significant amount is filtered in the glomeruli, on the other hand, a great part of it is reabsorbed by the proximal tubular cells (Campion *et al.*, 2017).

Most albuminuria is filtrated by the glomerulus and finally reabsorbed by the tubules. Albuminuria is considered as engrained indicator of glomerular destruction and has also been accepted as an indicator and independent risk factor for the progression of both cardiovascular disease (CVD) and renal in together the general population and the diabetic, albuminuria may play a vital role in the progression of renal disease (Matheson *et al*., 2010).

Albumin in urine is an essential element of diabetic nephropathy, it is essential to begin the description of the various grades of urine albumin excretion, normoalbuminuria is considered by a urine albumin excretion <30 mg/day, but microalbuminuria and macroalbuminuria mention to urine albumin excretion (UAE) of 30- 300 mg/day, and >300 respectively (Uwaezuoke, 2017).

Albuminuria can be measured in different methods:

1. Evaluating the amount of albumin in a 24-hours urine assembly has been considered the one of methods for the identification of diabetic nephropathy, assembling urine for 12 or 24 hour is hard in practice, and from time to time undependable if the urine sample is inadequate (Kim *et al.*, 2016).
2. The spot urine sample albumin-creatinine ratio (ACR) can be used in clinical situation to replace urinary albumin levels in a 24-hour urine assembly (Kim *et al.*, 2016).
3. Strip test albumin creatinine ratio was measured by a laboratory technician (Nah *et al.*, 2017).

CONCLUSION

Glomerular Filtration Rate (GFR) is one of the best-used indicators for diabetic nephropathy monitoring and diagnosis and should be estimated for all patients with diabetes mellitus, albuminuria and glomerular filtration rate might be mostly independent of each other, and glomerular filtration rate or albumin detection is inadequate to completely rise the present condition state of diabetic nephropathy, There was an association between age or BMI and albuminuria (nephropathy), so, age and BMI appear to have roles in the development of nephropathy. But there was no association between gender, duration of diabetes or smoking and albuminuria.

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