Predictors of Future Microalbuminuria in Type ١ Diabetes Mellitus

Thesis

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In Pediatrics

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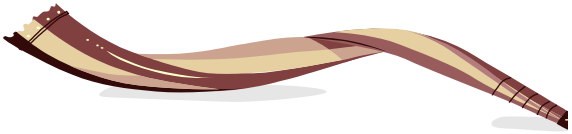

Sherine El Tokhy Ali

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List of Abbreviations

ACEI	Angiotensin-convering enzyme inhibitors
AER	Albumin excretion rate
AGE	Receptor for age
ARB	Angiotensin receptor blocker
BMI	Body mass index
BP	Blood pressure
DCCT	Diabetes control and complications trial
DM	Diabetes mellitus
DN	Diabetic nephropathy
DR	Diabetic retinopathy
EDIC	Epidemiology of diabetes interventions and complications
eGFR creat	Creatinine-based estimate of glomerular filtration rate
eGFR cyst	Cystatin c-based estimates of glomerular filtration rate
ESRD	End stage renal disease
GBM	Glomerular basement membrane
GFR	Glomerular filteration rate
HbA1C	Glycated hemoglobin
HDL	High density lipoprotein
Ht	Height
IUGR	Intrauterine growth retardation
LDL	Low density lipoprotein
MA	Microalbuminuria

NA	Normoalbuminuria
NAG	N-Acetyl-b-glucosaminidase
RBP	Retinol binding protein
T١DM	Type-١ diabetes mellitus
TG	Triglyceride
TNFa	Tumor necrosis factor alpha
TRF	Transferrin
UAE	Urinary albumin excretion
UAGT	Urinary angiotensinogen
Wt	Weight

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Abstract

Predictors of future microalbuminuria in type ١ diabetes mellitus:

This study aimed to follow diabetic patients who were normoalbuminuric but with increased levels of other nephropathy markers namely, (plasma homocystein, urinary n-acetyl-β-glucosaminidase, transferrin, alpha ١ micro globulin, retinol binding protein**)** for the lag period and the determinants to develop microalbuminuria.

Subject and Method: There were ٣٥ patients with type I diabetes mellitus who were enrolled, ٢٤ patients were normoalbuminuric at baseline .These patients were tested for other markers than urinary microalbumin to predict diabetic nephropathy and early renal impairment in children and adolescents with type ١ diabetes mellitus.

Result: Regarding the metabolic control between the studied groups we found that there is significant for HbA١C between the microalbuminuric patients compared to normoalbuminuric patients. According to number of positive markers of DN, the only parameter which was higher in patients with more than one marker elevated was mean SBP. Although mean DBP was higher, yet it was not statistically significant. Regarding to the predictability of urinary markers, urinary NAG is the most predictable marker with high sensitivity and specificity. The least sensitivity noticed was urinary RBP and the least specificity noticed was urinary alpha ١ microglobulin.

Conclusion: Urinary NAG is the most predictable marker with high sensitivity and specificity.

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Introduction

Type ١ diabetes mellitus (T١DM) is a multisystem disease with both biochemical and anatomical/structural consequences. It is a chronic disease of carbohydrate, fat, and protein metabolism caused by the lack of insulin, which results from the marked and progressive inability of the pancreas to secrete insulin because of autoimmune destruction of the beta cells **(Hovind et al., ٢٠١١).**

Type ١ DM can occur at any age. It occurs most commonly in juveniles but can also occur in adults, especially in those in their late ٣٠s and early ٤٠s **(Philippe et al., ٢٠١١)**.

Diabetic complications can be classified broadly as microvascular or macrovascular disease. Microvascular complications include neuropathy (nerve damage), nephropathy (kidney disease) and vision disorders (e.g. retinopathy, glaucoma, cataract and corneal disease). Macrovascular complications include heart disease, stroke and peripheral vascular disease (which can lead to ulcers, gangrene and amputation). Other complications of diabetes include infections, metabolic difficulties, impotence, autonomic neuropathy and pregnancy problems **(Philippe et al., ٢٠١١)**.

Diabetic nephropathy is one of the most common microvascular complications of diabetes mellitus, greatly affecting the life quality and survival of the patients. As global prevalence, the number of patients with diabetic nephropathy is expanding day by day **(Trachtman et al., ٢٠٠٦), (Perrin et al., ٢٠١٠)**. Diabetic nephropathy natural history is one of clinical silence for years to decades during which time serious underlying renal lesions may be developing. Once the clinical manifestations, including the development of persistent microalbuminuria are present, the structural injury is often far advanced. Since interventions at these late stages of disease may only slow but not completely arrest the inexorable progression towards renal failure, understanding early natural history becomes important **(Steinke et al., ٢٠٠٨)**.

Diabetic nephropathy, one of the leading causes of end stage renal disease, affects ٢٠ to ٣٠٪ patients with Type١ diabetes mellitus (DM). The course of diabetic nephropathy is slow. An increased urinary albumin excretion rate of ٣٠ to ٣٠٠ mg/٢٤ h (microalbuminuria) constitutes an early stage of nephropathy, especially when it becomes persistent (at least ٢ of ٣ consecutive urine samples. Annual screening for microalbuminuria should be initiated once the child is ١٠ years

of age and has had diabetes for ٥ years, more frequent testing is indicated if values are increasing **(Samanta et al., ٢٠١٢).**

Screening for subclinical retinopathy, neuropathy, and nephropathy should be started at puberty and at least ٣ years after the diabetes diagnosis with the goal of detecting early abnormalities responsible for subclinical disorders that can be reversed by improved metabolic control, thus preventing the occurrence of irreversible potentially incapacitating lesions **(Dorchy, ٢٠١٠).**

The association of well-established risk markers and promoters of renal injury, including degree and tracking of albuminuria, glycemic control, blood pressure changes, incipient retinopathy and genetic nephropathy and the decision to start pharmacological intervention **(Casani et al., ٢٠٠٠)**.

Increased urinary protein excretion in patients with diabetes has long been known to predict increased mortality, and its absence is associated with near-normal life expectancy. Recent studies confirmed and extended these findings by illustrating the progressive increase in mortality by degree of albuminuria. The excess mortality is due primarily to end stage renal disease and to cardiovascular disease, which share many risk factor **(Orchard et al., ٢٠١١).**

Urinary excretion of smaller molecular weight proteins such as n-acetyl-β-glucosaminidase (β-NAG) & retinol binding protein (RBP) **(Salem et al., ٢٠٠٢)**, alpha ١ microglobulin and transferrin (TRF) **(El-Habashy et al., ٢٠٠٢)** indicate proximal tubular dysfunction, and may identify diabetic patients at risk of developing diabetic nephropathy and may indicate the onset of microalbuminuria **(Mysliwiec et al., ٢٠٠٦).** Also, Plasma total homocystein rises with increased urinary albumin excretion in diabetes **(Tarnow et al., ٢٠٠١).**