Microalbuminuria Screening and Risk Factors in Adolescents with Type 1 Diabetes Mellitus In Zagazig University Hospital

Ayman Abd-Elrahman M.N.,Nagwa S Said,Mohammed S.S. Saad, Waseem M. Seleem, Magda M. Sherif [a] and Hanan Samir Ahmad [b]

[a] *Internal Medicine Department, and* [b] *Clinical Pathology Department, Zagazig University hospital, Egypt.*

ABSTRACT

BACKGROUND: Diabetic nephropathy (DN) is a leading cause of increased morbidity and mortality in adult patients with type 1 diabetes mellitus (T1DM). Microalbuminuria (MA) is an early marker for diabetic nephropathy, other microvascular and macrovascular diabetic complications. MA is rarely detected before puberty and the predictive value of MA for DN in adolescents with T1DM however is not well established. Although DN is rarely seen in adolescence, the dreadful complications originate in the early years of disease, even when the youth is still under pediatric care. **AIM OF THE STUDY**: Assessment of MA, the screening protocol, risk factors and health risks in adolescents with type 1 DM attending diabetes outpatient clinic in Zagazig University Hospital. **PATIENTS AND METHODS**: We screened 171 adolescents with T1DM,68 males (39.8%) and 103 females(60.2%) with mean age of 16.3±2 years and mean duration of diabetes of 9.7±2.3 years. They were fully evaluated clinically with revising their records regarding microalbuminurea, serum creatinine, glomerular filtration rate (GFR), glycosylated haemoglobin (HBA1c) and lipid profile. **RESULTS**:MA was present in 25 (14.6%) of the screened adolescents with T1DM, 6 males (24%) and 19 females (76%),while 146 patients (85.4%) revealed normoalbuminuria,62 males (42.5%) and 84 females (57.5%).MA was significantly associated with older age(20.1±5.1 years) with significant longer duration of T1DM (14.2±5.1 years) in comparison with normoalbuminuric group which revealed mean age (15.2±4 years) and mean duration (8.9±4.3years) (P<0.001). MA was significantly associated with hypertension (16%), short stature (32%) and limited joint mobility (LJM) (80%) versus (3%), (6.9%) and (57.5%) respectively in normoalbuminuric group (P<0.001). There was significant higher percent of patients with positive family history of hypertension (HTN) (32.0%) in microalbuminuric group compared to (13%) in normoalbuminuric group (P < 0.05). MA was associated with poor control of HBA1c, with statistically significant difference at 5 years after the onset of T1DM (9.8±2% gm versus 7.8±1.3 in normoalbuminimic group) and at 10 years (9.4±1.9% gm vs 7.6±0.9 in normoalbuminimic group) (P<0.001),but there were non-significant differences at 15 years and more between both groups. MA group also revealed significant decreased level of high density lipoprotein (HDL) (45.1±10 mg/dl versus 52±12.1mg/dl) (P<0.05) but no significant difference in other lipid parameters. No significant difference between both groups regarding gender, age of onset of diabetes, body mass index (BMI),daily insulin dosage, serum creatinine, GFR and family history of DM, cardiovascular or renal diseases. **CONCLUSIONS:** MA is present in 14.6% of adolescents with T1DM.MA is correlated with long duration of T1DM, HTN,family history of HTN, poor glycemic control, low HDL, short stature and limited joint mobility. Adolescents with T1DM have increased susceptibility to DN,and early screening of MA in adolescents with T1DM is a must for early intervention to prevent or delay the occurrence of DN.
Keywords: Diabetic nephropathy, microalbuminuria, type 1 diabetes mellitus.

INTRODUCTION

T1DM is the most common endocrine metabolic disorder of adolescence and accounts for 5-10% of all diagnosed cases of diabetes.[1]

Although data are limited, available information indicated that the prognosis in T1DM is poor in Arab countries, as a result of both acute and long-term complications.[2]

DN is a major cause of morbidity and mortality[3] and epidemiological studies have demonstrated that DN occurs in approximately one-third to one half of all patients with T1DM and today, diabetes is the most important cause of renal failure in the industrialized world.[4]

MA is a marker of early diabetic renal disease and is a harbinger of overt nephropathy, although it may regress in a substantial proportion of patients.[5] The risk factors for the development of DN or its progression in T1DM include gender, age of onset of diabetes, duration of disease, poor glycaemic control, blood pressure, lipids, central obesity and psychosocial and genetic factors.[6]

MA can be diagnosed from a 24-hour urine collection (between 30–300 mg/24 hours) or, more commonly, from elevated concentrations in a spot sample (30 to 300 mg/L). Both must be measured on at least two of three measurements over a two- to three-month period. An albumin level above the upper limit values is called "macroalbuminuria". To compensate for variations in urine concentration in spot-check samples, it is helpful to compare the amount of albumin in the sample against its concentration of creatinine. This is termed the albumin/creatinine ratio (ACR) and microalbuminuria is defined as ACR ≥ 3.5 mg/mmol in females or ≥ 2.5 mg/mmol in males.[7]

Increased urinary albumin excretion rate (AER) is widely accepted as the first clinical sign of DN. However, some diabetic patients could first manifest reduced glomerular filtration rate (GFR) or hypertension. Relatively advanced diabetic renal lesions can be present in some diabetic patients with long-standing normoalbuminuria, and this might indicate increased risk of progression to MA and then to overt DN.[8]

The prevalence of MA in adolescent with T1DM is reported to be between 7-20%, the exact value depending upon the cut off point for defining MA.[9]

In the adolescent population, MA detected in the first decade of disease will persist or progress in the second decade in approximately two thirds of patients and new MA will develop in a third of those initially normoalbuminuric.[10] This underlines the need for regular MA screening to be started early during this period.[11]

SUBJECTS AND METHODS

This is a cross sectional prospective study conducted on T1D patients attending Diabetes Endocrine Metabolic Unit (DEMU) in the Department of Internal Medicine, Zagazig University Hospital, between September 2011 and October 2012.the patients were 171,68 males (39.8%) and 103 females(60.2%) with mean age of 16.3±2 years and mean duration of diabetes of 9.7±2.3 years.

Eligible patients should have type 1 DM with minimum diabetes duration of 2 years at the time of enrollment and reaching the puberty with age from 11 years up to 21 years.

This study did not include patients with recent onset T1DM (< 2 years) and any patient younger than 11 years or older than 21 years. We also excluded presence of overt proteinuria, urinary tract infection, hematuria, ketonuria, pregnancy, acute febrile illness, heart failure, clinical conditions causing dehydration(due to possibility of false positive results on albumin measurements), any wasting disease that could cause severe undernourishment, after heavy exercise or heavy meal, and short–term pronounced hyperglycemia.

The study protocol was approved by institutional ethics committee and patients consented to participate in the study.T1D was diagnosed according to ADA criteria.[12]

Patients were subjected to the following assessment, including the use of review sheet where appropriate:

1. Full medical history taking and records review, laying stress on:
- Chronological age of the patient.
- Age at the onset of diabetes.
- Family history of diabetes, hypertension, renal or cardiovascular disease.
- Diabetes duration.
- Hospitalization for either hypo- or hyperglycemia during the past year.
- Insulin therapy during the last year; including:
  o The daily total dose of insulin (IU/kg/day).

o Number of daily injections received.
- History and data related to treatment for microalbuminuria or raised blood pressure.
- History and data related to any diabetic complications.
2. Thorough clinical examination including:
- Anthropometric measurements including: Obesity was evaluated by body mass index (BMI; mass kg/height m^2).
- Pubertal staging using the Tanner staging [13]
- Examination for the limited joint mobility by observation of the patient attempt to approximate the palmer surfaces of the interphalangeal joints.
- Passive examination is essential to confirm that inability to do is due to limited joint mobility (LJM).[14]
3. Revising follow up records checking for:
- Laboratory investigations including**:**
  o Urinary albumin excretion was assessed by early morning urine sample using Cobas 6000/Integra autoanalyzer (Roche, Germany), creatinine in urine was assessed using Cobas Integra 400 plus autoanalyzer (Roche, Germany),MA was defined as an ACR >2.5 mg/mmol in males or >3.5 mg/mmol in females, a repeat test was done 3 to 6 months after the first positive test for MA,and overt nephropathy was defined as an ACR > 30 mg/mmol.
  o Urine culture sensitivity and colony count to exclude urinary tract infections.
  o Serum creatinine by Cobas Integra 400 plus auto analyzer (Roche, Germany) and calculating the glomerular filtration rate (GFR) from the Schwartz formula:

Glomerular Filtration Rate (GFR): Schwartz formula was used in this study. Utilizing the proportionality between GFR and height/serum creatinine, Schwartz formula [11] was used to provide an estimate of GFR based on a constant multiplied by the youth's height divided by serum creatinine, thus:

$$C_{Cr} \text{ (ml/min/1.73 m}^2) = \frac{K \times height(cm)}{S_{Cr}(mg/dL)}$$

C$_{Cr}$: Creatinine clearance;**S$_{Cr}$:** Serum creatinine; **K**: Constant

The constant **K** is directly proportional to the muscle component of body, and varies with age and sex, the value of **K** to be used in premature infants is 0.45, in youth up to 13 years old is 0.55 and also in adolescent girls and boys the value of the constant changes to 0.7, normal GFR cutoff value ≥90 ml/min/ 1.73m^2.[15]
o HbA1c (by Cobas 6000/Integra auto-analyzer (Roche, Germany).
o Lipid profile including: serum triglycerides, total cholesterol, HDL and LDL by using Cobas Integra 400 plus autoanalyzer (Roche, Germany).

Statistical Analysis:
Data were tabulated and subjected to computer assisted statistical analysis using the statistical package for social science (SPSS) version 16.0.Means were compared using *t*-test and Pearson's correlations were used to explore associations between numerical variables. A p-value less than 0.05 were considered statistically significant, and less than 0.001 considered highly significant.

RESULTS
We invited a random sample of 171 patients [68 (39.8%) males and 103 (60.2%) females] coming from various areas from Sharkia Governorate, and having age ranged from 11 to 21 years. All patients were divided into two groups according to the results of ACR:

Group 1 or normoalbuminuric group: included 146 patients (85.4%) whose revealed normoalbuminuria, 62 males (42.5%) and 84 females (57.5%).

Group 2 or microalbuminuric group: included 25 patients with microalbuminuria (14.6%), 6 males (24%) and 19 females (76%).

The main baseline patients characteristics of both groups were compared and shown in table 1 which revealed that most of the patients included in this study within both groups were female, but no significant difference as regard gender between both groups (P > 0.05).

The microalbuminuric group had significantly older age (20.1±5.1 years) and longer disease duration (14.2±5.1 years) in comparison with normoalbuminuric group which has relative young age (15.2±4 years) and short

disease duration (8.9±4.3 years) (P <0.001).While there was a non-significant differences between the mean age of the onset of diabetes in microalbuminuric group (7.59±4 years) compared to normoalbumin-uric group (6.7±3.1 years) (P > 0.05) .

Our study showed no significant difference between microalbuminuric and normoalbuminuric group regarding BMI, (22.1±4 kg/m^2) and (21.5±5.1 kg/m^2) respectively (P > 0.05). Also there was no significant difference in daily insulin dosage, (1.1±5 IU/Kg/day) and (1±4 IU/Kg/day) respectively (P > 0.05).

These results found that short stature was significantly more likely in the microalbuminuric group (32.0%) than the normoalbuminuric group (6.9%), (p < 0.001).

The results showed statistical significant difference regarding limited joint mobility in microalbuminuric group (80%) compared to (57.5%) of the patients affected in normoalbuminuric group (p < 0.001).

The current study showed significant higher percent of patients with positive family history of HTN in microalbuminuric group (32.0%) compared to control group (13%) (p < 0.05), While higher percent of patients with family history of diabetes (36.0%), renal disease (4.0%) and cardiovascular disease (CVD) (4.0%) in the microalbuminuric group, compared to (26.0%), (0.0%) and (0.6%) respectively in normoalbuminuric group with no significant difference between both groups (P > 0.05).

Also there was higher percent of patients with high blood pressure in microalbuminuric group (16.0%) in comparison with normoalbuminuric group (3.0%) and that difference was statistically significant (p < 0.001), although there was higher percent of dyslipidemia (64.0%) in the microalbuminuric group, compared to (50.0%) in control group, there was no significant difference between both groups (P > 0.05).

The cumulative frequency of MA in the study group was represented in (**Table 2**) and it was 28 % at 5 years, 72% at 10 years, increasing to 92 % at 15 years.

Laboratory renal assessment including serum creatinine and estimated GFR of microalbuminuric and normoalbuminuric patients were assessed and showed that there was non-significant difference between both groups (P > 0.05) (**Table 3**).

Study of HbA1c of both groups revealed higher percent in microalbuminuric than normoalbuminuric patients and there was a statistically significant difference between both groups at 5 and 10 years after the onset of T1DM (P < 0.001), but, there was a non-significant difference at 15 years and more between both microalbuminuric and normoalbuminuric group (**Table 4**).

The lipid profile was assessed and showed that serum cholesterol, triglyceride (TG) and low density lipoprotein (LDL) were higher in the microalbuminuric group but the difference was not statistically significant (P > 0.05), while there was a statistically significant decreased level of HDL in microalbuminuric group in comparison with normoalbuminuric group (P < 0.05) (**Table 5**).

Table 1: Comparisons of baseline patients' characteristics between both groups:

	Normoalbuminuric group (n = 146)	Microalbuminuric group (n = 25)	P-Value
Gender Male (N & P) Female (N. & P)	62 (42.5%) 84 (57.5%)	6 (24.0%) 19 (76.0%)	0.08
Age (year) X±SD	15.2±4.0	20.1±5.1	< 0.001[*]
Duration (year) X±SD	8.9±4.3	14.2±5.1	<0.001[*]
Age at the DM onset X±SD	6.7±3.1	7.59±4.0	0.21
BMI X±SD	21.5±5.1	22.1±4.0	0.154
Insulin (IU/kg/day) X±SD	1±0.4	1.1±0.5	0.26
Short stature (N. & P)	10 (6.9%)	8 (32.0%)	< 0.001[*]
LJM (N.&P.)	84 (57.5%)	20 (80.0%)	< 0.001[*]
Family history DM (N. & P) HTN (N. & P) CVD (N. & P) Renal (N. & P)	39 (26.7%) 19 (13.0%) 1 (0.6%) 0 (0.0%)	9 (36.0%) 8 (32.0%) 1 (4.0%) 1 (4.0%	0.33 < 0.05[*] 0.06 0.14
Raised BP (N. & P)	5 (3.0%)	4 (16.0%)	< 0.001[*]
Dyslipidemia (N. & P)	73 (50.0%)	16 (64.0%)	0.19

N: Number. **P**: Percent [*]: significant (p < 0.05). **DM**: Diabetes mellitus. **BMI:** Body mass index. **LJM**:Limited joint mobility. **HTN**: Hypertension. **CVD**: Cardiovascular diseases. **BP**: Blood pressure.

Table 2: Cumulative rate of microalbuminuria in the **Microalbuminuric group:**

Disease duration	Frequency	Cumulative frequency	Percent
5 years	7	7	28
10 years	11	18	72
15 years	5	23	92
> 15 years	2	25	100

Table 3: Serum creatinine and estimated GFR with different diabetes duration in both groups:

Scr or GFR//Diabetes Duration	Normoalbuminuric group (n = 146)	Microalbuminuric group (n = 25)	P-Value
S_{Cr} (5 year)	0.65±0.2	0.66±0.1	0.53
S_{Cr} (10 year)	0.75±0.1	0.73±0.1	0.35
S_{Cr} (15 year)	0.78±0.1	1.1±1.0	0.21
S_{Cr} (>15 year)	0.8±0.5	0.76±0.2	0.4
GFR(5 year)	125.2±20	130±30	0.38
GFR(10 year)	127.2.6±22	129.2±31	0.57
GFR (15 year)	145.5±33	151.5±30	0.35
GFR(>15 year)	114±14	117±20	0.4
S_{Cr}increase/year	0.04±0.01	0.06±0.01	0.42

S_{Cr}: Serum creatinine   **GFR:** Glomerular filtration rate (normal: 90-150 ml/min/1.73m^2)

Table 4: HbA1c of normoalbuminuric and microalbuminuric groups:

Diabetes Duration	Normoalbuminuric group (n = 146)	Microalbuminuric group (n = 25)	P-Value
5 years	7.8±1.3	9.8±2	<0.001[*]
10 years	7.6±0.9	9.4±1.9	<0.001[*]
15 years	7.6±0.6	8 ±1.1	0.17
> 15 years	7.3±1.3	7.5±1.5	0.39

[*]: significant (p < 0.05)

Table 5: Lipid profile of normoalbuminuric and microalbuminuric groups:

Variable	Normoalbuminuric group (n = 146)	Microalbuminuric group (n = 25)	P-Value
Chol (mg/dl)	195±20	200±25	0.34
TG (mg/dl)	70±26	70.6±20	0.89
HDL (mg/dl)	52±12.1	45.1±10	<0.05[*]
LDL (mg/dl)	111±12	115±20	0.24
LDL/HDL	2.1±1.0	2.5±1.1	0.09

[*]: significant (p < 0.05) **Chol**: Cholesterol. **TG**: Triglycerides. **HDL**: High density lipoprotein. **LDL**: low density lipoprotein.

DISCUSSION

DN is the most important cause of increased morbidity and premature mortality in patients with T1DM. Detection of MA helps to carry out early interventions to halt the progression of early stages of diabetic nephropathy to advanced renal disease.[16]

Long-standing T1D patients with normal AER are still at risk of developing clinically significant nephropathy. It is therefore important to identify markers of increased nephropathy risk among these patients.[17]

The aim of the current study is to screen MA in adolescent patients with T1DM attending DEMU in Zagazig University Hospital, with evaluation of the association of MA with potential risk factors as age, gender, age at the onset of T1DM,duration of DM, family history

of related diseases, poor glycemic control, hypertension, dyslipidemia and LJM.

The current study was conducted on 171 adolescents with T1DM. Of those, 146 had normoalbuminuria(85.4%),this group males were (42.5%) and females (57.5%) and mean age was (15.2±4.0); while 25 patients (14.6%) had MA, in this group, males were (24%) and females (76%), and mean age of this sample was (20.1±5.1),with no significant difference as regard gender between both groups (P> 0.05).

These findings in agreement with **Soman and Soman**[18] who reported similar affection of both sexes, also, **Lindblad et al,**[19] found that albumin/ creatinine ratio was higher in females than in males before puberty but thereafter the rate become equal.

This prevalence of MA is compared to that previously reported which was 13.7% in 1994-1995,[20] and 13.3% in 2002-2003.[21]

In the current study, we found that there was increasing in disease duration in microalbuminuric group, there were (28%) of them at 5 years duration increasing to (72%) at 10 years duration. There was significant longer disease duration in microalbuminuric group, the mean age of duration disease (14.2±4.0 years) compared to (8.9±4.3 years) in normoalbuminuric group, (p < 0.001).This finding agree with the finding of **Bogdanovic,**[22] who found that the prevalence of MA increases steadily with time. This relationship between diabetes duration and persistent microalbuminuria among the adolescents seemed to arise from an excess of elevated UAE in patients undergoing pubertal growth and development and its attendant uncontrolled diabetes.

In our study, there was non-significant difference with the mean age of onset of diabetes in microalbuminuric group (7.59±4.0 years) compared to normoalbuminuric group (6.7±3.1 years) (P > 0.05). Also **Alleyn, et al**[23] concluded that, there were no differences in age, diabetes duration, BMI or BP percentile between those with and those without persistent MA.

As regards, there was non-significant difference with insulin dose in normoalbuminuric group compared to microalbuminuric group (P > 0.05).These results agree with **Perkins and colleagues**[24] who sought to study new-onset microalbuminuria, its progression, and the decline of renal function in patients with T1DM.They developed new-onset microalbuminuria in the first 4 years regardless of the daily insulin dosage.

In this study, we found statistical significant difference between both groups in short stature which more likely in the microalbuminuric group (32.0%) than the normoalbuminuric group (6.9%), (P < 0.001).

These results in agreement with the finding of **Ghaly et al,**[25] who found that short stature is associated with increased risk of developing DN. Also, those with more prolonged and less controlled diabetes may be more likely to suffer short stature.[14]

In the current study, LJM was significantly higher in the microalbuminuric group (80.0%) than the normoalbuminuric group (57.5%)   (P < 0.001).This finding in the agreement with **Kordonouri et al,**[14] who found that LJM is the earliest clinically apparent long-term complication of T1D in childhood and its associated with a 3-4 fold risk for nephropathy and neuropathy. However, the finding of 57.5% as the prevalence of LJM in the normoalbuminuric group is higher than the finding of **Kakourou et al,**[26] who found LJM in only 28.4%. This can be explained by that in **Kakourou's** study, the patients were younger and had shorter duration of diabetes (their age was 11.9±3.7 years) and duration of diabetes was 4.5±3.7 years compared by patients of our study, their mean age was 15.2±4 years and mean duration was 8.9±4.3 years. This suggests that LJM increases with age and duration of diabetes. Whether racial differences could be implicated needs further studies.

In our study, there was significant higher percent of patient with family history of hypertension in the microalbuminuric group (32%) compared to the normoalbuminuric group (13.0%) (P < 0.05) and raised BP in the microalbuminuric group (16.0%) compared to the normoalbuminuric group (3.0%)(P < 0.001). However there was non significant higher percent of patients with family history of DM

(36.0%) in MA group compared to (26.7%) in normoalbuminuric group (P > 0.05), also family history of renal disease had non significant higher percent in MA group (4.0%) compared to (0.0%) (P > 0.05), and non significant higher percent of the patient with family history of CVD (4.0%) in MA group compared to (0.6 %) in normoalbuminuric group (P > 0.05).

These finding is in the agreement with **Swierzewski,**[27] who found that, the presence of HTN in T1D patients means either the development of nephropathy or a significant risk to it. Furthermore, inadequately controlled BP increases the risk and rate of progression of nephropathy.[28]

Also, **Bain and Chwdhury,**[29]found that family history of DM, HTN, renal disease, and BP were higher in patients with increased ARE.

In this study, dyslipidemia was somewhat higher in the microalbuminuric group (64.0%) than in the normoalbuminuric group (50%) but the difference is not statistically significant (P > 0.05).While we found that there was significant difference in HDL between both groups (p < 0.05). This agrees with **Donaghue et al,**[30] who found that dyslipidemia is a risk factor for MA development. Moreover, the finding that half of our patients have dyslipidemia and also of those reported by **Jenkins et al,**[31] who found that 50% of the study group patients had dyslipidemia. This means that dyslipidemia is an additional risk for nephropathy; however, it is under treated.

In the present study, there was non-significant difference between the micro-albuminuric group and the normoalbuminuric group as regarding serum creatinine and GFR. Only one patient of the microalbuminuric group passed into stage 4 DN and experienced progressive decline in the GFR with progressive rise in the serum creatinine and blood urea nitrogen. We found that there was non-significant difference between both groups (P > 0.05).This can be explained by that the duration of diabetes in the study group patients were not enough to show this progression and the impairment of the kidney functions; however, **Swierzewski,** [27] found that patients with DN will pass through five predictable stages.

In the current study, HbAlc was significantly higher in patients with MA (9.8±2.0) compared to normoalbuminuric group (7.8±1.3) in patients with 5 years of diabetes duration and (9.4±1.1) in MA group compared to (7.6±0.9) in normoalbuminuric group in patients with 10 years of diabetes duration, (P < 0.001). Also, we found that there was non-significant difference in HbAlc after 15 years, and more of diabetes duration (P > 0.05). This agrees with the finding of **DCCT,**[32] that has shown that there is a strong association between poor metabolic control and the development of diabetic complications. Also this agrees with the recommendation of **Rewers et al,**[33] that recommends HbAlc target range for all age groups of < 7.5%. As teens approach adulthood, lower targets similar to those of the adult population were suggested (< 7.0%), recognizing that the hormonal alterations and psychological adjustments of adolescence make achieving these targets difficult.

Similarly**, Alleyn and colleagues,**[23] calculated 2 year mean data for HbA_{1c} and blood pressure to assess exposure to factors known to be related to UAE, not unexpectedly, elevated HbA1c was significantly associated with persistent microalbuminuria, the mean 2 year HbA_{1c} was 9.1% in the young people with persistently elevated UAE compared to 8.7% in those with normal UAE. Data from adolescents aged 13–17 years at entry into the Diabetes Control and Complications Trial demonstrate the importance of blood glucose control for the development of microvascular complications; a 40% risk reduction for the development of microalbuminuria was experienced in the intensively treated group compared with the conventionally treated group[34,35].

The feasibility and long-term additional benefits of lowering targets merit further study and each adolescents should have their targets individually determined with the goal of achieving a value as close to normal as possible while avoiding severe hyperglycemia as well as frequent mild to moderate hypoglycemia.[29,31.]

Perkins et al,[36] found regression to normoalbuminuria in 40–60% of patients in a study of 400 adolescents with Type 1 DM and microalbuminuria. Other Study in children and

adolescents have demonstrated similar regression rates of 32–58%.[37]

Similarly, **Steinke et al,**[38] followed 178 patients with Type 1 DM for 5 years; all patients were normoalbuminuric at baseline. Of the 22 patients who met criteria for persistent microalbuminuria at some point during the follow-up period, 14 patients (64%) had reverted to normoalbuminuria and eight patients (36%) still had persistent microalbuminuria at the end of the study; treatment with ACE inhibitors was not a significant predictor of regression. **Gorman et al,**[39] found a 32% rate of regression over 6 years in adolescents who had MA at baseline.

Bogdanovic,[22] found that micro-albuminuria does not necessarily progress to persistent protenuria. The elevated ARE may occur transiently or intermittently and in a considerable number of patients (40-50%) may regress to normal. MA can also regress, especially in adolescents.

In conclusion: MA is present in 14.6% of adolescents with T1DM.MA is correlated with long duration of TIDM,HTN,family history of HTN, poor glycemic control, low HDL, short stature and limited joint mobility. Adolescents with T1DM have increased susceptibility to DN, and early screening of MA in adolescents with T1DM is a must for early intervention to prevent or delay the occurrence of DN.

REFERENCES

1. **Shalitin S, Peter Chase H:** Diabetes technology and treatments in the pediatric age group. Int J Clin Pract Suppl. **2011**; (170):76-82.
2. **de Boer IH, Rue TC, Cleary PA, Lachin JM, Molitch ME, et al:** Long-term renal outcomes of patients with type 1 diabetes mellitus and microalbuminuria: an analysis of the diabetes control and; Trial/Epidemiology of Diabetes Interventions and Complications cohort. Arch Intern Med.**2011**; 171(5):412-20.
3. **Thorn LM, Forsblom C, Fagerudd J, Thomas MC, Pettersson-Fernholm K, Saraheimo M, et al:** Groop P-H on behalf of the Finn-Diane study group: Metabolic syndrome in type 1 diabetes. Association with diabetic nephropathy and glycaemic control (the Finn Diane Study).Diabetes Care. **2005**; 28:2019–24.
4. **Al-Habeeb QS, Tawfik HA, Al-Eidani HR:** Early detection of diabetic nephropathy in children and adolescents with type 1 diabetes mellitus. DMJ **2008**; 2(1):91-106.
5. **Perkins BA, Ficociello LH, Roshan B, Warram JH, Krolewski AS:** In patients with type 1DM and new-onset microalbuminuria, the development of advanced chronic kidney disease may not require progression to proteinuria. Kidney Int.**2010**; 77(1):57-64.
6. **Stone ML, Lee JW, Craig ME, Verge CF, Chan AK, Donaghue KC:** Natural history and risk factors for microalbuminuria in adolescents with type 1 diabetes. Diabetes Care. **2006**; 29:2072–7.
7. **Al-Kateb H, Boright AP, Mirea L, Xie X, Sutradhar R, Mowjoodi A, et al:** Multiple superoxide dismutase 1/splicing factor serine alanine 15 variants are associated with the development and progression of diabetic nephropathy. The diabetes control and complications trial/epidemiology of diabetes interventions and complications genetic study. Diabetes. **2008**; 57: 218–28.
8. **Caramori ML, Fioretto P, Mauer M:** Low glomerular filtration rate in normoalbuminuric type 1 diabetic patients: an indicator of more advanced glomerular lesions.Diabetes,**2003;** 52(4):1036-40.
9. **Abdul-Rasoul M, Habib H, Al-Khouly M:** "The honeymoon phase" in children with type 1 diabetes mellitus: frequency, duration, and influential factors. Pediatr Diabetes, **2006;** 7:101–107.
10. **Cobas RA, Santos B, da Silva B, et al:** Progression to microalbuminuria in patients with type 1 diabetes: a seven-year prospective study. Diabetology & Metabolic Syndrome, **2011**; 3:21.
11. **Samanta D, Mallika V and Yadav S:** Early microalbuminuria in adolescent Type 1 diabetic patients: Experience from a pediatric endocrine clinic in a developing country.

Journal of Diabetes and Endocrinology, **2012;** 3(1):6-10.

12. **The Expert Committee on the Diagnosis and Classification of Diabetes mellitus.** Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care. **1997**; 20:1183–97.

13. **Tanner JM, Whitehouse RH:** Clinical longitudinal standards for height, weight, height velocity, and stages of puberty. Arch Dis Child, **1979;**51:170-9.

14. **Kordonouri O, Maguire AM, Knip M, et al:** Other complications and conditions associated with diabetes in children and adolescents. Pediatric Diabetes, **2009;** 10(12):204-210.

15. **Schwartz JG and Work DF:** Measurement and Estimation of GFR in Children and Adolescents. CJASN, **2009**; 11:1832-43.

16. **Atiya JK, Hassan MK and Al-Naama LM:** Microalbuminuria in children and adolescents with type 1 diabetes mellitus. MJBU, **2007**; 25, (2):5-11.

17. **Chowta NK, Pant P, Chowta MN:** Microalbuminuria in diabetes mellitus; Association with age, sex, weight, and creatinine clearance. Indian Journal of Nephrology, **2009**; 19,(2):53-56.

18. **Soman SS and Soman AS:** Diabetic Nephropathy: Treatment and Medication, **2009;** from http://emedicine.medscape.com/ article/238946-overview.

19. **Lindblad BA, Maynard C and Boyko EJ:** Racial differences in diabetic nephropathy, cardiovascular disease and mortality in a national population of veterans. Diabetes Care, **2003;** 26:2392-99.

20. **Marcovecchio ML, Tossavainen PH and Dunger DB:** Status and rationale of renoprotection studies in adolescents with type 1 diabetes. Pediatr Diabetes. **2009**; 10:347–355.

21. **Salah N, Hassan F, Hassan M, Abdel-Hamid A:** Microalbuminuria in type 1 diabetics: Risk factors, progression and prevention. M.Sc. Thesis in pediatrics, Cairo University, **2004;** 80-111.

22. **Bogdanovic R:** Diabetic nephropathy in children. Nephrol Dial Transplant, **2001;** 16 (6):120-2.

23. **Alleyn CR, Volkening LK, Wolfson J, Rodriguez-Ventura A, Wood JR, and Laffel LMB:** Occurrence of microalbuminuria in young people with Type 1 diabetes: importance of age and diabetes duration. Diabet Med. **2010**; 27(5): 532–537.

24. **Perkins BA, Ficociello LH, Roshan B, Warram JH and Krolewski AS:** In patients with type 1 diabetes and new-onset microalbuminuria the development of advanced chronic kidney disease may not require progression to proteinuria. Advanced chronic kidney disease risk in microalbuminuria. Kidney International **2010**; 77:57-64.

25. **Ghaly I, Salah N, El-Moughy F, Hafez M, Attia M, Hassan M:** Microalbuminuria in insulin dependent diabetes mellitus. Journal of Arab Child, **1995;** 6:291.

26. **Kakourou T, Dacou-Voutetakis C, Kavadias G, et al:** Limited joint mobility and lipodystrophy in children and adolescents with insulin-dependent diabetes mellitus. Pediatr Dermato, **1994;** 11 (4):310-4.

27. **Sweirzewski ST:** Diabetic nephropathy, **2001;** from:http://www.nephrologychannel. com/diabetic nephropathy/index.shtml.

28. **Lurbe E, Redon J, Kesani A, Pascual JM, Tacons J, Alvarez V, Batlle D:** Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. N Engl J Med, **2002;** 347:797–805.

29. **Bain SC and Chowdhury TT:** Genetics of diabetic nephropathy. Journal of the Royal Society of Medicine, **2000;** 93.

30. **Donaghue KC, Chiarelli F, Trotta D, et al:** Microvascular and macrovascular complications associated with diabetes in children and adolescents. Pediatric Diabetes, **2009;** 10(12): 185-203.

31. **Jenkins AJ, Lyons TJ, Zhen GD, et al:** DCC/EDIC Research Group: Serum lipoproteins in the diabetes control and complications trial/epidemiology of diabetes intervention and complications cohort:

associations with gender and glycemia. Diabetes Care, **2003;** 26 (3):810-8.

32. **DCCT:** Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes control and complications trial. Diabetes control and complications trial research group. J Pediatr, **1994;** 125:177-88.

33. **Rewers A, Klingensmith G, Davis C, et al:** Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth: the search for diabetes in youth study. Pediatrics, **2008;** 121 (5):1258-66.

34. **The Diabetes Control and Complications Trial Research Group.** The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. **1993**; 329:977–986.

35. **Diabetes Control and Complications Trial Research Group.** Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. J Pediatr.**1994**; 125:177–188.

36. **Perkins BA, Ficociello LH, Silva KH, Finkelstein DM,Warram JH, Krolewski AS:** Regression of microalbuminuria in type 1 diabetes. N Engl J Med. **2003**; 348:2285–2293.

37. **Amin R, Widmer B, Prevost AT, Schwarze P,Cooper J, Edge J, et al:** Risk of microalbuminuria and progression to macroalbuminuria in a cohort with childhood onset type 1 diabetes: Prospective observational study. BMJ. **2008**; 336:697–701.

38. **Steinke JM, Sinaiko AR, Kramer MS, Suissa S, Chavers BM, Mauer M, et al:** The early natural history of nephropathy in Type 1 Diabetes: III. Predictors of 5-year urinary albumin excretion rate patterns in initially normoalbuminuric patients. Diabetes. **2005**; 54:2164–2171.

39. **Gorman D, Sochett E, Daneman D:** The natural history of microalbuminuria in adolescents with type 1 diabetes. J Pediatr. **1999**; 134:333–337.