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Correlation of Microalbuminuria with Glycosylated Hemoglobin (Hba1c) and Duration of Type 2 Diabetes Mellitus (T_2DM) in Male and Female Patients

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Abstract: Long term irregularity in glycemic state, especially in Type 2 diabetes mellitus (T_2DM) patients, depicted by higher levels of HbA1c, is noted to be correlated with development of microalbuminuria. Present study was undertaken to investigate the association of urinary microalbuminuria with HbA1c and with duration of diabetes mellitus in male and female T_2DM patients. This cross-sectional study was carried out in a total of sixty patients, thirty each males and females with diagnosed T_2DM, within age group of 31-55 years. Biochemical parameters of urea, creatinine, urinary micro albumin, HbA1c, fasting blood glucose and post-prandial blood glucose were determined by standard methods. Data was statistically examined by student's t-test and Pearson's correlation. Results comparison with healthy control subjects depicted significantly elevated levels of all parameters in both male and female T2DM patients ($P < 0.05$ to $P < 0.001$). Comparison of duration of T_2DM with existence of urinary micro albumin was moderately significant ($P < 0.05$) when duration was less than 4 years, significant ($P < 0.01$) with duration of 4-6 years and markedly significant ($P < 0.001$) with duration of more than 6 years. Conclusion; it was concluded in our study that with male and female T_2DM patients, duration of DM as well as poor glycemic control, depicted by higher levels of HbA1c is significantly correlated with elevated levels of urinary micro albumin.

Key words: Type 2 Diabetes Mellitus · Glycosylated Hemoglobin · Urinary Micro albumin

INTRODUCTION

Recent and past studies have reiterated that development of microalbuminuria is a common risk factor for onset of macro-vascular diseases, end stage renal disease and related complication in Type 2 diabetes mellitus (T_2DM) [1-5]. Moreover, T2DM itself is a major cause of nephropathy as reported by several studies from many countries [3, 4 &6] including Pakistan [1]. To monitor progress and adherence to glycemic control in diabetes mellitus (DM), one of the major and commonest parameter is HbA1c. This glycosylated hemoglobin can also be used to predict preceding physiological complication and most importantly development of nephropathy in T2DM patients [2, 7]. Previous studies have reported a positive correlation between microalbuminuria and elevated HbA1c in diabetic patients [3, 7-9]. However, none of the studies detailed the pattern or extent of microalbuminuria correlation with HbA1c, neither impact of duration of T_2DM and microalbuminuria, individually, in male and female T_2DM patients.

Present study described the association of urinary microalbuminuria with HbA1c and with duration of DM in male and female T_2DM patients.

MATERIALS AND METHODS

Study Protocols and Patients' Selection: This cross-sectional study was carried out at department of Biochemistry lab services-Liaquat National Hospital, Departments of Chemical Pathology and Biochemistry, Nephrology and Endocrinology, Liaquat National Hospital and Medical College-Karachi during the period Dec 2012 to Dec 2014. A total of sixty patients, thirty each males and females of diagnosed T_2DM, within age group

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of 31-55 years were included in the study. Age-matched sixty healthy, thirty each of male and female were taken as controls. Inclusion criteria was patients (thirty each) of either gender, diagnosed with T2DM, age greater than 30 and less than 55 years, routinely visited clinics and adhered to periodic check-ups and analyses of prescribed parameters, such as urea, creatinine, urinary microalbumin, HbA1c, fasting blood glucose (FBG) and post- prandial blood glucose (PPBG). Exclusion criteria were patients with smoking habits, surgeries, cardiac ailments, on statins, aged less than 31 and greater than 55 years.

Analytical Methods: Micro albumin was determined in 2nd morning urine by TINA-QUANT (Roche-Diagnostics) albumin methodology [10] and HbA1c in whole blood by TINIA TINA-QUANT Gen 3 method [11]. Blood was collected from patients for analyzing either plasma FBG or PPBG, plasma urea and creatinine. Glucose was determined by Gluco-quant-hexokinase method [12] whereas urea and creatinine by UV-urease [13] and Jeff's rate-blanked method [14] respectively.

Statistical Analysis: This cross-sectional study was statistically analyzed by student's t-test to find the significance of parameters, whereas Pearson's correlation was used to evaluate duration of T_2DM and HbA1c levels with microalbuminuria.

RESULTS

Results are summarized in Table 1-4. In males T_2DM patients, FBG was 160.30 ± 21.46 mg/dl (Table 1) whereas in females it was slightly higher 184.45 ± 20.75 mg/dl (Table 2). Similarly PPBG, HbA1c, urinary microalbumin, urea and creatinine in male T2DM were 234.45 ± 32.20 mg/dl, 8.10 ± 3.65%, 101.24 ± 24.55 mg albumin/g creatinine, 56.60 ± 10.10 mg/dl and 1.40 ± 0.80 mg/dl, respectively, whereas in female the results were on slightly higher side except creatinine as 265.65 ± 30.40 mg/dl, 8.75 ± 4.64%, 111.55 ± 29.55 mg albumin/g creatinine, 49.70 ± 11.30 mg/dl and 1.36 ± 0.70 mg/dl, respectively.

Comparison with healthy control subjects depicted significantly elevated levels of all parameters in both male and female T_2DM patients ($P < 0.05$ to $P < 0.001$). Comparison of duration of T_2DM with existence of urinary microalbumin was moderately significant ($P < 0.05$) when duration was less than 4 years (Tables 3, 4). However urinary albumin was noted be significant ($P < 0.01$) in patients with duration of T_2DM between 4-6 years and markedly significant ($P < 0.001$) in patients where duration was greater than 6 years.

Finally, it was also noted that HbA1c levels, that were slightly higher in females than males, showed significant correlation with duration of T_2DM, in similarity with urinary microalbumin.

Table 1: Mean levels of biochemical parameters in type 2 diabetic male patients (n = 30) and control subjects (n = 30)

Parameters	Control subjects	Patients	P value (<0.05)
FBG (mg/dl)	86.10 ± 8.75	180.30 ± 21.46	< 0.001
PPBG (mg/dl)	111.20 ± 18.25	234.45 ± 32.30	< 0.001
HbA1c (%)	5.10 ± 0.45	8.10 ± 3.65	< 0.001
Urinary micro albumin (mg/g creatinine)	10.86 ± 5.20	101.24 ± 24.55	< 0.001
Urea (mg/dl)	21.25 ± 4.50	56.60 ± 10.10	< 0.01
Creatinine (mg/dl)	0.80 ± 0.30	1.40 ± 0.80	< 0.05

Results are expressed as Mean ± SD

Table 2: Mean levels of biochemical parameters in type 2 diabetic female patients (n = 30) and control subjects (n = 30)

Parameters	Control subjects	Patients	P value (<0.05)
FBG (mg/dl)	80.20 ± 9.70	184.45 ± 20.75	< 0.001
PPBG (mg/dl)	110.35± 19.70	265.65 ± 30.40	< 0.001
HbA1c (%)	5.54± 0.70	8.75 ± 4.64	< 0.001
Urinary micro albumin (mg/g creatinine)	9.70 ± 5.70	111.55 ± 29.65	< 0.001
Urea (mg/dl)	19.10 ± 5.75	49.70 ± 11.35	< 0.01
Creatinine (mg/dl)	0.57 ± 0.20	1.36 ± 0.70	< 0.05

Results are expressed as Mean ± SD

Table 3: Duration of Type 2 diabetes in male patients (n = 30) and correlation with the presence of microalbuminuria

Duration of diabetes	Urinary micro albumin (mg albumin/g creatinine)	P value (< 0.05)
1-2 years	76.35 ± 8.90	< 0.05
2-4 years	98.50 ± 11.65	< 0.05
4-6 years	108.45 ± 10.55	< 0.01
> 6 years	150.60 ± 20.75	< 0.001

Results are expressed as Mean ± SD

Table 4: Duration of Type 2 diabetes in female patients (n = 30) and correlation with the presence of microalbuminuria

Duration of diabetes	Urinary micro albumin (mg albumin/g creatinine)	P value (< 0.05)
1-2 years	85.40 ± 9.55	< 0.05
2-4 years	101.40 ± 12.05	< 0.05
4-6 years	110.45 ± 11.35	< 0.01
> 6 years	162.35 ± 21.30	< 0.001

Results are expressed as Mean ± SD

DISCUSSIONS

This study highlighted the relationship of duration of T_2DM with urinary micro albumin and consequent correlation with higher level of HbA1c in both male and female T_2DM patients. Previous studies had established the notion that elevated levels of urinary micro albumin, which is an indicator of renal anomalies and diabetic nephropathy, is associated with poor glycemic control, evident by higher levels of HbA1c [2, 3&7-9]. Present study also indicated that long-term association with T_2DM, with consequent poor glycemic control, eventually created onset of diabetic nephropathy, indicated by higher microalbuminuria, supported by higher plasma levels of urea and creatinine. Our findings are in agreement with other findings, both recent and past, that suggested independent predictive efficacy of HbA1c for development of micro-albuminuria in patients with T_2DM [1, 2 &7] and in T_1DM as well [4,15].

Moreover earlier studies reported prevalence of microalbuminuria in T_2DM at 34% [1] supported by other studies from subcontinent [8, 16]. Furthermore, as observed in our study, higher levels of microalbuminuria was found associated with duration of T_2DM [16, 17] and noted to be due to poor glycemic control over a period of 2-4 years [17]. It is documented that development of chronic complications, such as diabetic nephropathy, depends on duration of DM and concomitant inadequate glycemic monitoring, depicted by higher levels of HbA1c [2,18 & 19]. It is therefore recommended that in patients with T_2DM, yearly detection of urinary micro albumin for assessment of proper renal function and HbA1c for evaluation of appropriate glycemic control, should be followed dynamically [2, 20].

Unlike, previously reported studies [3, 5] our study showed a slightly higher level of urinary micro albumin (but non-significant by comparison) in females as compared to males. This might occurred due to inclusion of more females with longer duration of T_2DM, such as more than 6 years with poor glycemic control (Table 4). However, since both gender exhibited higher levels of urinary micro albumin, this manifested respective development of diabetic nephropathy. Earlier studies in T_2DM patients suggested strong correlation of proteinuria and development of renal failure [21].

CONCLUSIONS

Finally, in our study with male and female T_2DM patients, duration of DM as well as poor glycemic control, depicted by higher levels of HbA1c was significantly correlated with elevated levels of urinary micro albumin. It is thus suggested that annual determination of urinary micro albumin, especially in patients with longer duration of T2DM, should be done mandatorily. Secondly, counseling patients to adhere to proper glycemic management, would also provide positive outcome and ultimate reversal of suspected diabetic nephropathy, as constantly elevated HbA1c is associated with development of proteinuria in T_2DM patients.

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