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Correlation of Microalbuminuria with Glycated Hemoglobin, Blood Pressure and Duration of Diabetes

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Abstract

Objective: Correlation of Microalbuminuria with Glycated Hemoglobin, Blood Pressure and Duration of Diabetes.

Methods: A total of one hundred and twenty five subjects were included in the study, out of which hundred non-insulin dependent diabetic patients were selected from diabetic clinic, and various medical units of Jinnah Postgraduate Medical Center Karachi and twenty five non diabetic healthy subjects were included in the control group. All the selected patients were grouped on the basis of duration of diabetes and the level of microalbuminuria. Groups on the basis of duration of diabetes and Groups on the basis of level of microalbuminuria.

Results: In the present study, the Comparison of age, weight, height, body mass index and duration of diabetes of control with group A, B, C and D of patient's changes were not significant. Mean systolic blood pressure of group C and D was significantly high ($p<0.01$) when compared with control subjects, while the mean arterial pressure of group D was also found significantly high ($p<0.05$) in group D when compared with control subjects. The fasting serum glucose and glycated hemoglobin levels of group A, B, C and D were significantly high ($P<0.001$) in contrast to control subjects. Systolic blood pressure of group C was significantly high ($P<0.05$) when compared with group A. The values of glycated hemoglobin in group B, C and D were significantly greater ($P<0.01$, <0.01 and <0.001, respectively) when compared to group A, whereas the values were significantly. The mean values of systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting serum glucose and glycated hemoglobin levels of control and group I, II and III. The systolic blood pressure of group III was observed significantly high ($P<0.01$) as compared to control subjects. The fasting serum glucose and glycated hemoglobin levels of group I, II and III were significantly high ($P<0.001$) in contrast to control. While systolic blood pressure and mean arterial pressure of group III ($P<0.01$ and <0.05, respectively) and diastolic blood pressure, mean arterial pressure and glycated hemoglobin of group II were observed significantly high ($P<0.05$), when compared with group.

Conclusion: Improving the glycemic control, maintaining the blood pressure and early diagnosis of the disease may reduce the risk of development and progression of microalbuminuria and ultimately end stage renal damage and mortality.

Keywords: Microalbuminuria; Glycated hemoglobin; Blood pressure; Duration of diabetes

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Introduction

Microalbuminuria is an established predictor of the later development of nephropathy in insulin dependent and non-insulin dependent diabetes [1] and of infarction and cardiovascular mortality [2]. It precedes the development of nephropathy and is at present the first abnormality that clearly allows an early identification of patients susceptible to the developing nephropathy. Diabetic microalbuminuria is defined as "sub-clinical" albuminuria, that is, excretion rates of albumin, which are abnormally elevated but not detectable by routine laboratory procedures [3]. In normal glomeruli neutral substances with effective molecular diameter less than 4 nm are freely filtered while that of more than 8 nm is not. The sialoproteins in glomerular capillary walls are negatively charged, and negative charges repel the negatively charged substances in blood, with the result that the filtration of anionic substances is less than half that of neutral substances of same size, this is why the albumin, with effective molecular diameter of approximately 7 nm is not filtered [4]. In the healthy kidney over 99% of filtered albumin is reabsorbed. A small increase in glomerular vascular permeability results in an increase in filtered albumin presented to the renal tubules. This cannot be reabsorbed and results in an increase in urinary albumin [5]. There are no striking differences in the nephro-pathological changes accompanying IDDM compared with NIDDM. The earliest pathological change is an increase in thickness of the glomerular basement membrane, a thickening of the capillary wall and an increase in the mesangial volume relative to glomerular volume [2-5]. This basement membrane thickening in the glomeruli causes increased permeability of the filtration barrier and leads to microalbuminuria [6]. The pathogenesis of microalbuminuria in diabetes is clearly multifactorial. Altered composition of extracellular matrix has been reported. Patients with IDDM and microalbuminuria have been shown to have increased transcapillary albumin permeation in variety of tissues including kidneys, and a variety of pathogenic mechanisms have been proposed to explain this, including loss of negatively charged heparin sulfate proteoglycan [7]. The primary and most important cause of microalbuminuria in diabetes is an early phase of diabetic nephropathy. However, it should be stressed that there are a number of other factors that enhance albumin and protein excretion, in normal persons as well as in diabetics [4]. Several modifiable risk factors for the development and progression of microalbuminuria, such as poor glycemic control, slightly increased blood pressure, smoking, hyperlipidemia, and strict metabolic control have been identified [5]. Nakano et al. in 1998 have also demonstrated these factors along with progressed diabetic microangiopathy as risk factors for vascular events in diabetic subjects, making it crucial, to control these risk factors to prevent various vascular events. The cumulative probability of developing microalbuminuria during childhood is related to sex, glycemic control, and duration of diabetes. Although these factors affect the prevalence of microalbuminuria in childhood, the cumulative probability is similar irrespective of age at diagnosis, indicating the importance of glycemic control and diabetes duration in the prepubertal years. Both poor control of diabetes and high blood pressure, are associated with a high urinary albumin excretion in diabetes [4-10]. Increased Blood Pressure: is a major determinant in the progression towards end-stage renal failure. Numerous cross sectional studies have shown that microalbuminuria is associated with the increased blood pressure. It affects the progression of microalbuminuria to overt proteinuria in NIDDM; especially systolic blood pressure has a positive influence on the progression of microalbuminuria [8]. It is well established that overt proteinuria in type I diabetes is associated with elevated blood pressure and early mortality. Effective antihypertensive treatment has been shown to slow the progression of diabetic renal disease [4]; especially angiotensin converting enzyme (ACE) inhibitors have been shown to slow the rate of deterioration of albumin excretion rate and creatinine clearance in normotensive microalbuminuric NIDDM, although the superiority of ACE inhibitors over other antihypertensives that has been demonstrated in IDDM has not been confirmed in NIDDM [11]. There is controversy as to whether an increase in blood pressure precedes or is a result of the development of microalbuminuria [8]. Glycemic control: is the most potent contributor to the development of microalbuminuria. The secondary complications of diabetes are highly correlated with long term control of blood glucose level. The findings of Diabetes Control and Complication Trial performed by American Diabetes Association in 1993 clearly demonstrate a close relation between the quality of glycemic control and the incidence and progression of diabetes specific-complications. Determination of glycated hemoglobin is considered a useful index of long term glycemic control, and the test is now routinely used to monitor diabetic control [9]. In recently conducted prospective studies it is proved that glycated hemoglobin is a significant predictor for incidence of infarction and cardiovascular mortality in patients with NIDDM [10]. There is evidence of a close relationship between poor glycemic control and progression of microalbuminuria to early nephropathy, most authorities aim for tight glycemic control, especially in young patients [11]. Jones et al, in 1998 have confirmed the association of persistently raised urinary albumin excretion with poorer glycemic control early in the disease. Improving glycemic control might reduce the incidence of microalbuminuria in early IDDM. Several proteins undergo post-ribosomal non-enzymatic glycosylation *in vivo* and *in vitro*. In this reaction, glucose attaches to proteins via free amino group at the N-terminus or ξ-amino group of lysine residue, forming a stable ketoamine derivative. The interaction of glucose with protein is a condensation reaction in which the degree of glycosylation is proportional to the ambient glucose concentration; this process is enhanced in the diabetic state with attendant hyperglycemia. The proteins subject to increased glycosylation include hemoglobin, albumin, erythrocyte membrane proteins and lens crystalline and aortic collagen [8]. Human adult hemoglobin (Hb) usually consist of HbA (α2β2) 97%, HbA_2 (α2δ2) 2.5% and HbF (α2γ2) 0.5% of total hemoglobin. Chromatographic analysis of HbA identifies a number of minor hemoglobins, HbA_{1a}, HbA_{1b} and HbA_{1c}, which are collectively referred to as HbA_1. HbA consists of four polypeptide chains, two α−chains and two β-chains. HbA_{1c} is formed by the condensation of glucose with the N-terminal valine of each β-chain of HbA to form an unstable Schiff base

(aldimine, pre-A_{1c}), which then under goes an amadori rearrangement to form a stable ketoamine, HbA_{1c}. It is the major fraction, constituting approximately 80% 0f HbA_1 [11]. The measurement of glycated hemoglobin (HbA_{1c}) is considered a useful index of long term glycemic control, and provides an integrated, retrospective index of glucose control, reflecting the mean glucose concentration over six to eight weeks before the measurement and the test is now routinely used to monitor diabetic control [8]. Increased duration of diabetes: increases the incidence and frequency of microalbuminuria in patients with non-insulin dependent diabetes [12]. Microalbuminuria appears more prevalent in some ethnic groups [13]. Its prevalence in non-insulin dependent diabetes mellitus is estimated to be 20 to 30 % higher in Asians than in Europeans [14]. Because the evolution of the diabetic cardiovascular and renal disease is potentially modifiable, investigation of determinants of microalbuminuria is important [15]. Therefore we intend to see the various proposed risk factors, which predispose non-insulin dependent diabetic patients to the development of microalbuminuria. In diabetic patients mortality rates increases excessively with the onset and progression of microalbuminuria, which precedes the development of diabetic nephropathy. To prevent the development of microalbuminuria may prevent the diabetic nephropathy and end-stage renal damage. Keeping in view these facts we intend to evaluate the relation of certain risk factors for development of microalbuminuria in our study. Therefore the aim of the present study was to find out the correlation of microalbuminuria with glycated hemoglobin, blood pressure and duration of diabetes.

Material and Methods

The proposed study was carried out in the Department of Biochemistry, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center, Karachi. A total of one hundred and twenty five subjects were included in the study, out of which hundred non-insulin dependent diabetic patients were selected from diabetic clinic, and various medical units of Jinnah Postgraduate Medical Center Karachi and twenty five non diabetic healthy subjects were included in the control group. All the selected patients were grouped on the basis of duration of diabetes and the level of microalbuminuria.

Groups on the basis of duration of diabetes

- Group A: Patients having diabetes ≤ 5 years.
- Group B: Patients having diabetes from 6 to 10 years.
- Group C: Patients having diabetes from 11 to 15 years.
- Group D: Patients having diabetes >15 years.

Groups on the basis of level of microalbuminuria

- Group I: Patients having UAER from 21 to 120 µg/min.
- Group II: Patients having UAER from 121 to 170 µg/min.
- Group III: Patients having UAER from 171 to 200 µg/min.

Collection of blood sample

Ten ml blood was drawn from each patient included in the study, in the morning after an overnight fast (12-14 h) by venepuncture using plastic disposable syringes under aseptic measures. 1 ml aliquot was added in the bottle containing anticoagulant EDTA that was used for the determination of glycated hemoglobin (HbA_{1c}). The remaining blood was allowed to clot at 37°C and serum was separated by centrifugation within an hour of blood collection and glucose determination was done immediately. Remaining serum was stored at -20°C for subsequent analysis. Before analysis, the samples were allowed to attain the room temperature.

Determination of glycated hemoglobin (HbA_{1c})

Glycated hemoglobin (HbA_{1c}) was estimated by the ion-exchange-colorimetric method, using kit Cat. No. 10 658 supplied by Human, Germany.

Principle

Whole blood is hemolyzed with a lysing reagent containing detergent and a high concentration of borate ions to cause the elimination of labile schiff's base. The hemolysate is then mixed for 5 min with a weekly binding cation exchange resin. During this time hemoglobin in the hemolyzed sample is bounded by the cation-exchange resin. By means of a special resin separator, the resin is being separated from the supernatant fluid containing HbA_{1c}. The percentage of the glycated hemoglobin is determined by measuring the absorbance of the HbA_{1c} fraction and total hemoglobin against water at 415 nm in comparison with a standard glycated hemoglobin preparation carried through the test procedure.

Procedure

A. Hemolysate preparation

1) 100 µl of the well-mixed blood sample and standard was mixed into correspondingly labelled tubes containing lysing reagent.
2) The tubes were incubated for 15 min at room temperature

B. Glycated hemoglobin separation

1) 100 µl from each of the above hemolysate was added to a well-mixed ion exchange resin tube having homogenous resin suspension.
2) Resin separator was inserted and positioned in the tube 1 cm above the ion exchange resin solution and the tubes were shaken for 5 min.
3) The resin separators were then pushed into the tubes until the ion exchange resin was firmly packed.
4) The absorbance of HbA_{1c} of the supernatant was measured against water as blank at 415 nm in Bausch and Lomb Spectronic 20 Spectrophotometer.

C. Total hemoglobin

1) 20 µl from each of the above hemolysate was mixed to 5 ml of distilled water in appropriately labeled test tubes.
2) The absorbance (A) of total Hb was measured against water as blank at 415 nm in Bausch and Lomb Spectronic 20 Spectrophotometer.

Determination of Microalbuminuria

The microalbuminuria was estimated by colorimetric "Pyrogallol-Red" method, using kit Cat. No. 100 1025 supplied by Spinreact, S.A. Spain.

Principle

The reaction between the protein and Pyrogallol-Molybdate, form a red complex. The intensity of the color is directly proportional to the albumin concentration.

Procedure

1. The blank, standard and urine sample tubes were prepared as shown in table.
2. The contents of the tubes were mixed thoroughly and incubated for 10 min at room temperature.
3. The absorbance (A) of the standard and the sample were measured against the blank at 598 nm in Bausch and Lomb Spectronic 20 Spectrophotometer. The color was stable for 30 min.

	Blank	Standard	Sample
Standard	----------	40 µl	----------
Sample	----------	----------	40 µl
Working Reagent	2.00 ml	2.00 ml	2.00 ml

Results

Table 1 shows mean values and comparison of age, weight, height, body mass index and duration of diabetes of control with group A, B, C and D of patients. While **Table 2** shows the inter-group comparison of these parameters. When age, weight, height and body mass index of control subjects were compared with all groups of patients, non-significant changes were seen. Whereas in **Table 2** mean age of group D was significantly higher ($p<0.05$) when compared with group A and B and mean body mass index of group C was significantly high ($p<0.05$) when compared with group B. Mean duration of diabetes was highly significantly more in group B, C and D in comparison with group A ($p<0.001$). **Tables 3 and 4** shows the mean values of systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting serum glucose and glycated hemoglobin levels of control and group A, B, C and D and their comparison. Mean systolic blood pressure of group C and D was significantly high ($p<0.01$) when compared with control subjects, while the mean arterial pressure of group D was also found significantly high ($p<0.05$) in group D when compared with control subjects. The fasting serum glucose and glycated hemoglobin levels of group A, B, C and D were significantly high ($P<0.001$) in contrast to control subjects. Systolic blood pressure of group C was significantly high ($P<0.05$) when compared with group A. The values of glycated hemoglobin in group B, C and D were significantly greater ($P<0.01$, <0.01 and <0.001, respectively) when compared to group A, whereas the values were significantly. **Table 5 and 6** shows the mean values of systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting serum glucose and glycated hemoglobin levels of control and group I, II and III. The systolic blood pressure of group III was observed significantly high ($P<0.01$) as compared to control subjects. The fasting serum glucose and glycated hemoglobin levels of group I, II and III were significantly high ($P<0.001$) in contrast to control. While systolic blood pressure and mean arterial pressure of group III ($P<0.01$ and <0.05, respectively) and diastolic blood pressure, mean arterial pressure and glycated hemoglobin of group II were observed significantly high ($P<0.05$), when compared with group I.

Discussion

Non-insulin dependent diabetic subjects have higher morbidity and mortality for various vascular events than does those in general population. Cerebrovascular and renal diseases related to the progression of atherosclerosis are well known to be the frequent cause of death [16] and microalbuminuria has been shown to predict increased morbidity and early mortality in non-insulin dependent diabetes mellitus [17]. In a ten year prospective study in insulin dependent diabetes mellitus, performed by Mathiesen and his associates a close relation between long term glycemic control and development of microalbuminuria was found [18]. It is believed that poor metabolic control is the most important factor in the development of microalbuminuria. Similar results were observed by Microalbuminuria Collaborative Study Group, United Kingdom [19]. In their follow up study they recruited 137 insulin dependent diabetic patients for 4 years. Out of these 137 patients eleven developed persistent microalbuminuria, giving rise a cumulative frequency of 8%. Patients who developed persistent microalbuminuria had significantly raised blood pressure and glycated hemoglobin at base line ($P<0.05$) and remained higher throughout the study period. It was reported that glycemic control is the most potent contributor to development of microalbuminuria and hypertension affects the progression of microalbuminuria to overt proteinuria [20]. They studied 74 normoalbuminuric and 49 microalbuminuric patients, their results showed high mean glycated hemoglobin levels in group who developed microalbuminuria than who remained normoalbuminuric ($P<0.01$) inspite no significant difference in the mean blood pressure, while in group who developed overt proteinuria from microalbuminuria in the six years follow up period, showed high mean arterial pressure, than who remained microalbuminuric ($P<0.01$) inspite of no significant difference in mean glycated hemoglobin.

In our study, the mean value of glycated hemoglobin was significantly high ($P<0.001$) in all groups of patients when compared with control subjects having mean glycated hemoglobin 6.00 ± 0.13. It was also significantly high in group II and III having glycated hemoglobin 11.11 ± 0.44 and 11.29 0.28 respectively in comparison to group I, having 9.32 ± 0.60

Table 1 Comparison of systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting serum glucose and glycated hemoglobin levels of control and groups of patients with non-insulin dependent diabetes mellitus on the basis of duration of diabetes.

Variable	Control (25)	Group A (25)	Group B (25)	Group C (25)	Group D (25)
SBP (mm Hg)	124.20 ± 2.85	130.40 ± 4.06	127.20 ± 2.97	** 140.40 ± 4.45	** 137.80 ± 3.68
DBP (mm Hg)	82.00 ± 1.23	84.80 ± 2.53	82.60 ± 2.00	82.20 ± 2.06	82.60 ± 1.58
MAP (mm Hg)	96.05 ± 0.44	100.00 ± 2.79	97.47 ± 2.12	101.60 ± 2.53	* 101.01 ± 1.82
FSG (mg/dl)	91.12 ± 1.31	*** 165.88 ± 12.68	*** 174.04 ± 12.38	*** 189.84 ± 15.38	*** 184.60 ± 12.49
Hb A_{1c}(%)	6.00 ± 0.13	*** 8.95 ± 0.47	*** 10.66 ± 0.45	*** 11.36 ± 0.46	*** 12.03 ± 0.35

* P<0.05, ** P<0.01, *** P<0.001 as compared to control
SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; FSG: Fasting Serum Glucose; HbA_{1c}: Glycated hemoglobin

Table 2 Comparison of systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting serum glucose and glycated hemoglobin levels among groups of patients with non-insulin dependent diabetes mellitus.

Variable	Group A (25)	Group B (25)	Group C (25)	Group D (25)
SBP (mm Hg)	130.40 ± 4.06	127.20 ± 2.97	† 140.40 ± 4.45	137.80 3.68
DBP (mm Hg)	84.80 ± 2.53	82.60 ± 2.00	82.20 ± 2.06	82.60 ± 1.58
MAP (mm Hg)	100.00 ± 2.79	97.47 ± 2.12	101.60 ± 2.53	101.01 ± 1.82
FSG (mg/dl)	165.88 ± 12.68	174.04 ± 2.38	189.84 ± 15.38	184.6 ± 12.49
Hb A_{1c} (%)	8.95 ± 0.47	** 10.66 ± 0.45	** 11.36 ± 0.46	†*** 12.03 ± 0.35

**P<0.01, *** P<0.001 as compared to group A, † P<0.05 as compared to group B

Table 3 Comparison of age, weight, height, body mass index, and duration of diabetes of control and groups of patients with non-insulin dependent diabetes mellitus on the basis of microalbuminuria.

Variable	Control (25)	Group I (25)	Group II (25)	Group III (50)
Age (Years)	50.56 ± 1.79	* 44.64 ± 1.47	49.76 ± 1.82	53.60 ± 1.06
Weight (Kg)	62.84 ± 1.81	62.48 ± 2.44	67.36 ± 2.26	67.90 ± 1.78
Height (m)	1.56 ± 0.03	1.55 ± 0.02	1.61 ± 0.02	1.59 ± 0.01
BMI (Kg/m^2)	25.99 ± 0.56	25.92 ± 0.80	26.01 ± 0.91	26.66 ± 0.58
Duration (Years)	-----	5.36 ± 0.79	8.60 ± 0.89	13.40 ± 0.75

* P<0.05 as compared to control; BMI: Body Mass Index

Table 4 Comparison of age, weight, height, body mass index, and duration of diabetes among groups of patients with non-insulin dependent diabetes mellitus on the basis of microalbuminuria.

Variable	Group I (25)	Group II (25)	Group III (50)
Age (Years)	44.64 ± 1.47	* 49.76 ± 1.82	*** 53.60 ± 1.06
Weight (Kg)	62.48 ± 2.44	67.36 ± 2.26	67.90 ± 1.78
Height (m)	1.55 ± 0.02	1.61 ± 0.02	1.59 ± 0.01
BMI (Kg/m^2)	25.924 ± 0.802	26.008 ± 0.910	26.662 ± 0.581
Duration (Years)	5.36 ± 0.79	*** 8.60 ± 0.89	*** 13.40 ± 0.75

*P<0.05, *** P<0.001 as compared to group I; BMI: Body Mass Index

(P<0.05), which shows the relationship of glycated hemoglobin. These results are in agreement with the different studies [21-26]. In our study we have observed a significantly high levels of fasting blood glucose (P<0.001) in all the groups when compared to control subjects, which are in consistent with the results of Park [13] who also studied non-insulin dependent diabetic patients. The results of Powrie [18] also showed the high base line plasma glucose concentration and glycated hemoglobin concentration in patients who developed microalbuminuria than who remained normoalbuminuric (P<0.001). Gall et al. performed a prospective study of 176 normoalbuminuric non-insulin dependent diabetic patients under 66 years of age in Denmark and reported that the long term poor glycemic control and hyper cholesterolemia were potent risk factors for the development of incipient and overt nephropathy [26]. In their study high systolic blood pressure at base line was also observed in patients who developed nephropathy than in the patients who remained normoalbuminuric. Our study also resembles to that of Gall's study, because, we have also recruited non-insulin dependent diabetic patients having age limit upto 65 years. In the study of John and his associates, during the five years observation period, they observed higher systolic blood pressure during follow up in the progresses; suggest a positive correlation between systolic blood pressure and the progression of microalbuminuria. The association of hypertension and albuminuria has been recognized by many other workers. Abuaisha et al. also showed the significant higher prevalence of hypertension in microalbuminuric patients 62% versus 38% in normoalbuminuric patients (P<0.05) [1]. Our results also show the significant high mean systolic blood pressure, 138.00 ± 2.62 in patients of group III, when compared with control subjects and patients of group I having mean systolic pressure 124.20 ± 2.85 and 125.40 ± 3.89 respectively (P<0.01),

Table 5 Comparison of systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting serum glucose and glycated hemoglobin levels of control and groups of patients with non-insulin dependent diabetes mellitus on the basis of microalbuminuria.

Variable	Control (25)	Group I (25)	Group II (25)	Group III (50)
SBP (mm Hg)	124.20 ± 2.85	125.40 ± 3.89	134.40 ± 3.99	** 138.00 ± 2.62
DBP (mm Hg)	82.00 ± 1.23	79.80 ± 2.32	85.80 ± 2.07	83.30 ± 1.32
MAP (mm Hg)	96.05 ± 1.44	95.00 ± 2.48	102.00 ± 2.47	101.54 ± 1.46
FSG (mg/dl)	91.12 ± 1.31	*** 162.96 ± 15.74	*** 178.12 ± 13.26	*** 186.64 ± 8.30
Hb A_{1c} (%)	6.00 ± 0.13	*** 9.32 ± 0.60	*** 11.11 ± 0.44	*** 11.29 ± 0.28

** P<0.01, *** P<0.001 as compared to control

Table 6 Comparison of systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting serum glucose and glycated hemoglobin levels among groups of patients with non-insulin dependent diabetes mellitus on the basis of microalbuminuria

Variable	Group I (25)	Group II (25)	Group III (50)
SBP (mm Hg)	125.40 ± 3.89	134.40 ± 3.993	** 138.00 ± 2.62
DBP (mm Hg)	79.80 ± 2.32	85.80 ± 2.07	83.30 ± 1.32
MAP (mm Hg)	95.00 ± 2.48	* 102.00 ± 2.47	* 101.54 ± 1.46
FSG (mg/dl)	162.96 ± 15.74	178.12 ± 13.26	186.64 ± 8.30
Hb A_{1c} (%)	9.32 ± 0.60	* 11.11 ± 0.44	* 11.29 ± 0.28

*P<0.05, **P<0.01 as compared to group I

which is in agreement with results of Gall and John. The mean arterial pressure in our study was also significantly raised in group II and III 102.00 ± 2.47 and 101.54 ± 1.46 in comparison to group I having 95.00 ± 2.48 (P<0.05), which suggest that the mean arterial pressure affects the progression of microalbuminuria. Similar results were observed in insulin dependent diabetes mellitus by Microalbuminuria Collaborative Study Group, who reported that arterial blood pressure, the main predictor of progression of microalbuminuria to overt proteinuria. The incidence of microalbuminuria rises with increasing duration of diabetes. Powrie et al. in their study in insulin dependent diabetic patients have observed some predictive value of long duration of diabetes for the development of microalbuminuria, which was also reported by Microalbuminuria Collaborative Study Group in 1993 [18]. The above results were confirmed by John et al. They found the influence of duration of diabetes on progression of microalbuminuria (P<0.01), this shows that as the duration of diabetes increases, UAER also increases. These results were confirmed by Niskanen et al. who found the increased incidence of microalbuminuria between 5 and 10 years of duration of diabetes [27].

Conclusion

In conclusion we have observed the association of poor glycemic control, increased blood pressure, and long duration of diabetes with the development and progression of microalbuminuria in non-insulin dependent diabetes, which has been recognized as a powerful and independent marker of diabetic nephropathy, infarction and cardiovascular mortality. Improving the glycemic control, maintaining the blood pressure and early diagnosis of the disease may reduce the risk of development and progression of microalbuminuria and ultimately end stage renal damage and mortality.

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