Effect of Allopurinol Versus Angiotensin Converting Enzyme Inhibitors in Decreasing Microalbuminuria in Type I Diabetic Patients

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INTRODUCTION

• Diabetic nephropathy is a major microvascular complication of diabetes. It affects 25-35% of diabetic patients diagnosed under the age of 30 years. It is the leading cause of premature death in young diabetic patients . The development of diabetic nephropathy is a complex pathology, however many studies demonstrated that serum uric acid levels in the high normal range are strong predictor of the development of albuminuria in patients with type 1diabetes . The inflammatory role of uric acid in tubular epithelial cell was also confirmed by an in vitro study in which uric acid directly induced ICAM-1 expression in human proximal tubular cells and may induce oxidative stress.

AIM OF THE WORK

• This study was primary designed to assess the short -term effect (6 months) of allopurinol treatment compared to angiotensin-converting enzyme inhibitor (ACEI) and placebo in type 1 diabetic patients (T1DM) with microalbuminuria .

SUBJECTS AND METHODS

 Subjects: The present study included 90 (46 males and 44 females) type 1 diabetic adolescents who were recruited from the regular attendants of the Pediatric Diabetes Clinic, Children's Hospital, Ain Shams University over 10 months period . **Inclusion criteria** included: adolescents with T1DM, less than 18 years with diabetes mellitus more than 5 years ,microalbuminuria positive twice repeated monthly and absence of systemic diseases or other causes of proteinuria based on physical examination and history **Exclusion criteria** included : Uncontrolled diabetes, hypertension, fever in the past 1 month, urinary tract infection (UTI),development of allopurinol side effects e.g.: (elevated liver enzymes, cytopenia & dermatitis). Patients were divided into the following groups:
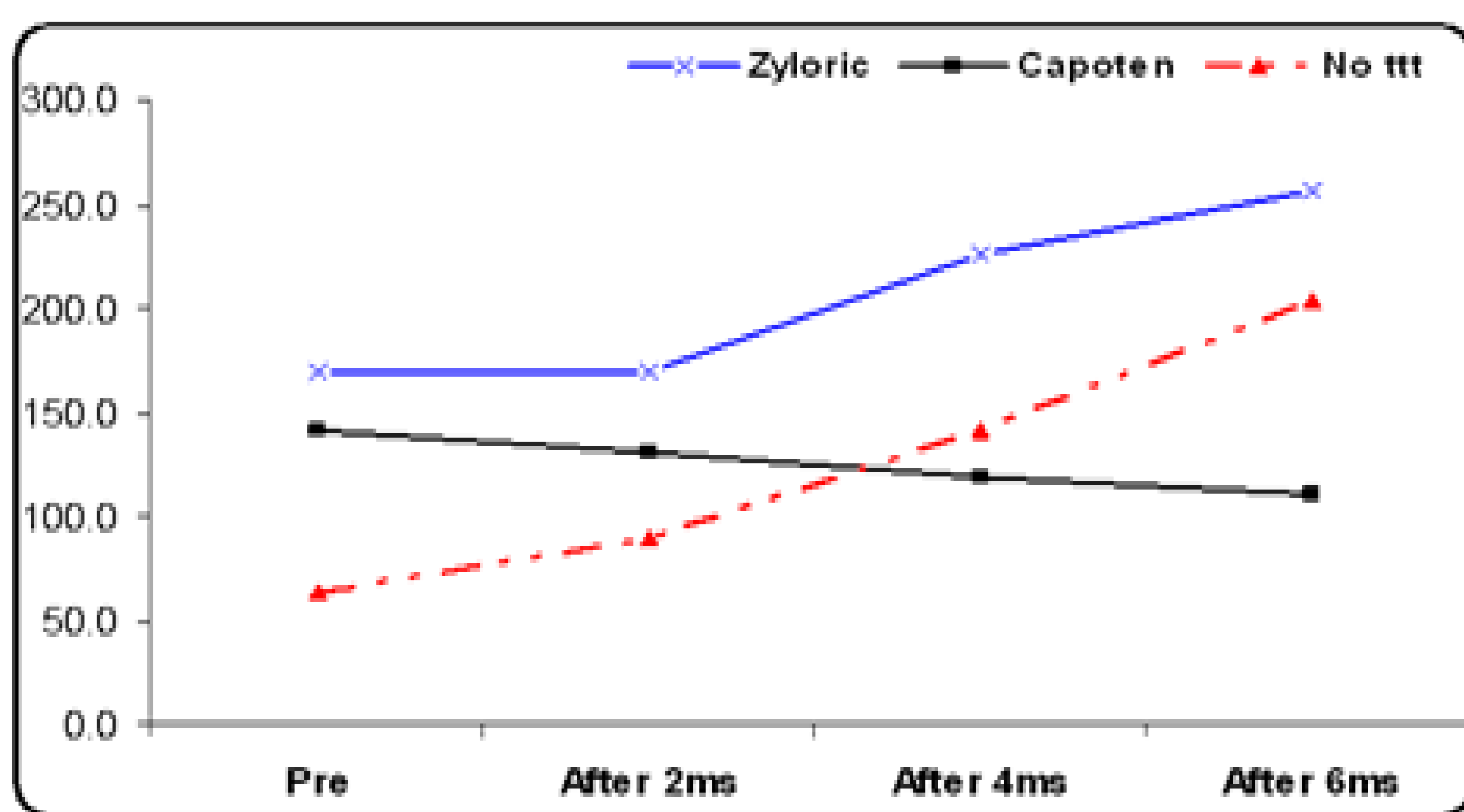**Group A:** Patients who received allopurinol (zyloric 100 mg tablet),Dose: 100 mg/day/every 24 hours not related to meal.
Group B: Patients who received Angiotensin Converting Enzyme Inhibitors (ACEI) Capoten 25 mg tablet with a dose of : 1 mg/kg dose every 12 hours .
Group C : Patients who did not receive any medications for microalbuminuria and served as a control group.
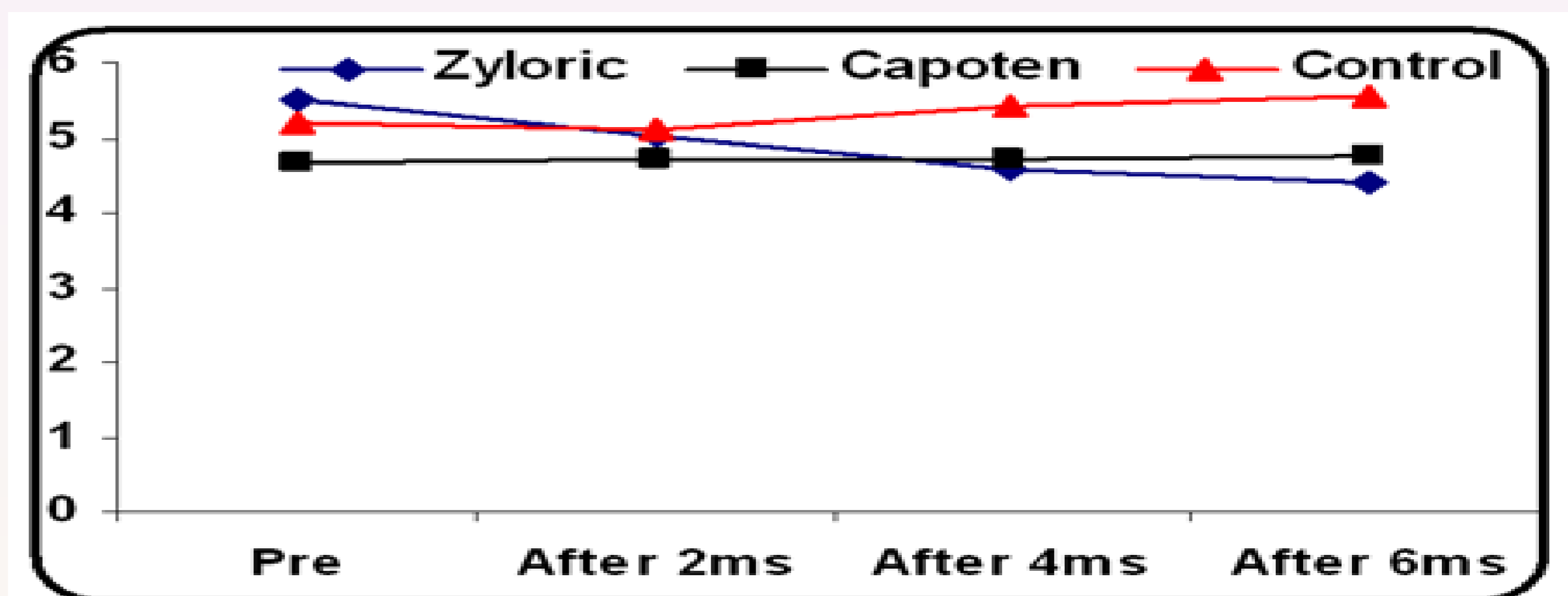**Methods :**All subjects underwent the following:
Detailed Questionnaire : Complete history taking including their age, diabetes duration, complications, insulin regimen. **-Clinical assessment:** Physical examination includes: anthropometric measures; weight in kg , height in cm and body mass index (BMI); blood pressure . **-Investigations:** HbA1C , fasting and 2 Hours post prandial blood sugar ,CBC, Blood urea nitrogen (BUN) (mg/dl),Serum uric acid (mg/dl),Serum total proteins and serum albumin (mg/dl),Serum potassium (mmol/L),serum Alanine aminotransferase (mg/dl), micro-albumin in urine(mg/g creatinine) **-Follow up:** Patients were followed up at 2-4-6 month respectively by comparing all studied parameters.
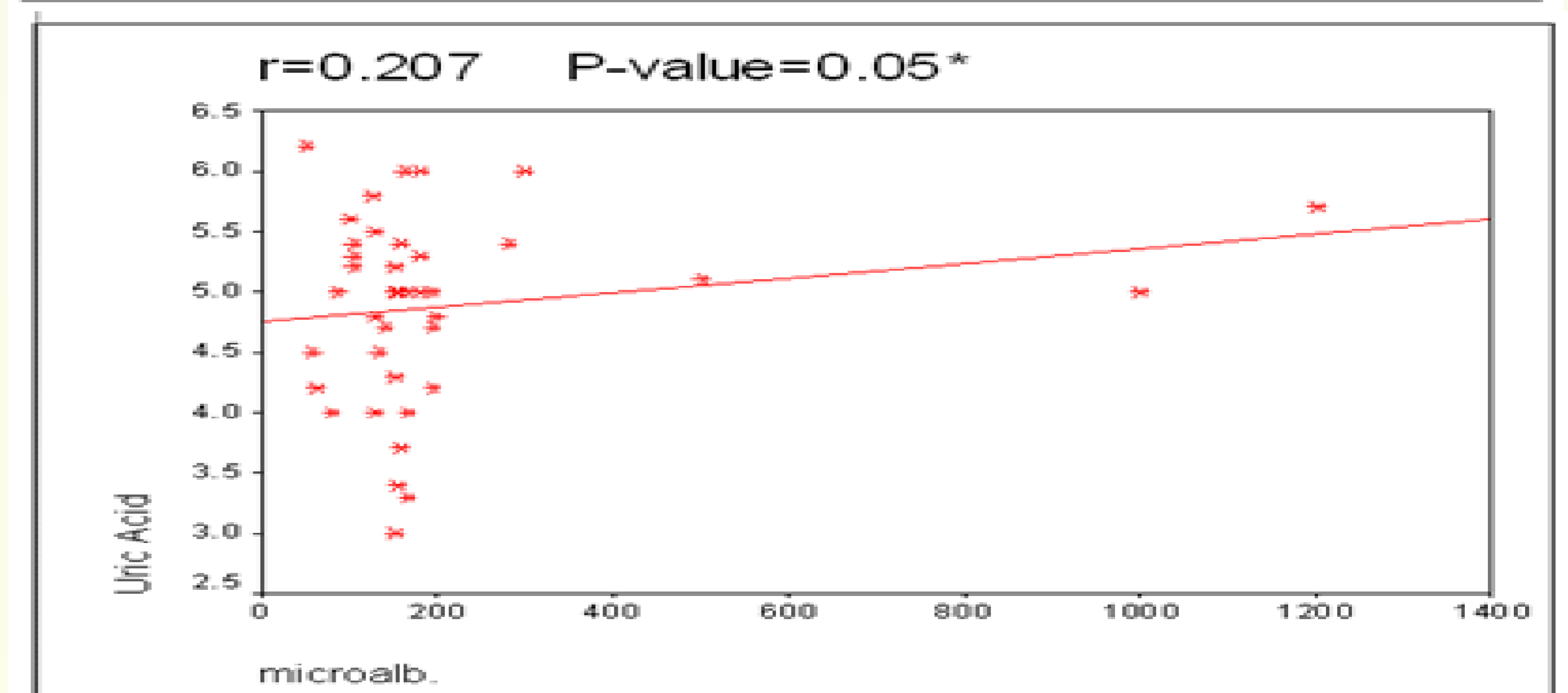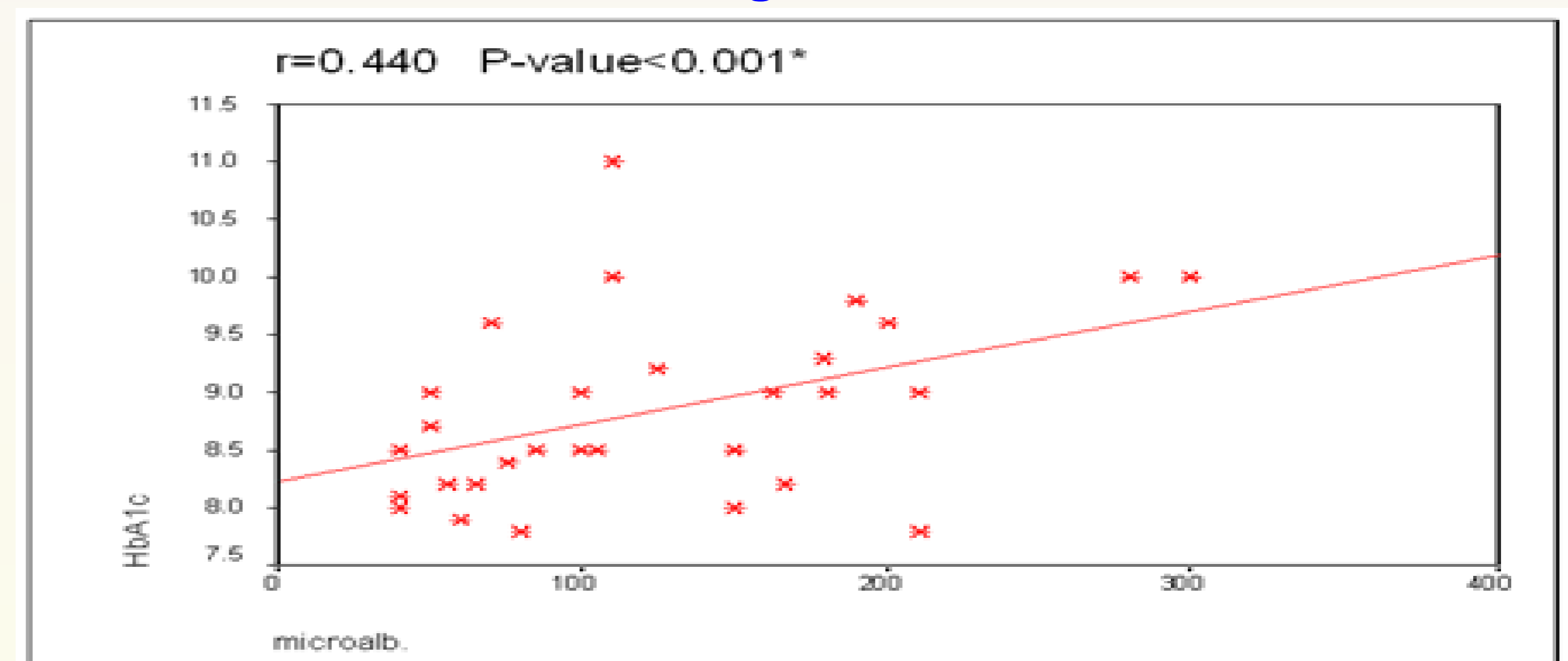
Fig(1):   Comparison between patients received zyloric, capoten & control group as regards microalbuminuria at baseline which was assessed again at 2, 4 & 6 months

RESULTS

• Patients' aged 8.0-18.0 years (mean age 13.183 ± 2.526 years with diabetes lasting for 8.867±2.260 years (range 5-13) and mean microalbuminuria was 124.600 ± 70.193 (mg/l) , all participants were on intensive insulin therapy.
• After 6 months of receiving treatment ; the microalbuminuria level did not change significantly either in the allopurinol group or in control group(p=0.124,P=0.891 respectively) Fig(1).
• ACEI proved to be superior to both in improving microalbuminuria (P=0.000). Serum levels of uric acid were significantly lower in the patients on allopurinol tablets (*P* = .02) whereas other groups showed increase in its level(P=0.38 p=0.24 respectively) Fig(2).
• There were positive correlations between Hb1Ac (r = 0.440, P= 0.001), FBS (r = 0.375, P = 0.001), duration of diabetes (r = 0.968 , P < 0.001) , blood pressure (r = 0.232, P = 0.028)and microalbuminuria. A borderline correlation between uric acid & microalbuminuria was found (r = 0.207, P = 0.050) that emphasizing on the role of uric acid in pathogenesis of DN (Fig3).
• No Side effects of medication were observed apart from mild increase in ALT levels in 13% of patients who received allopurinol(*P* = .004).

Fig(2) :Comparison between patients received zyloric, capoten & control group as regards serum uric acid at baseline which was assessed again at 2, 4 & 6 months

Fig(3):Correlation between microalbuminuria , HbA1c and uric acid

CONCLUSION

❖ **Our data implicate that low-dose allopurinol was not effective in reducing microalbuminuria after 6 months of drug administration.**
❖ **Combination strategy should thus be a more effective tool for obtaining optimal control in patients with diabetic nephropathy.**