

EFFICACY OF ANTI-HYPERTENSIVE IN PROLONGING DIABETIC NEPHROPATHY

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ABSTRACT

The main focus of our study is to know the efficacy of different classes of antihypertensive and there combinations like Angiotensin receptor blockers, β -blockers, Calcium channel blockers, ACE inhibitors in prolonging diabetic nephropathy. The study includes 49 subjects of type 1 and 2 diabetes each. The data was collected from a designed data collection form in diabetic nephropathy patients who are on anti-hypertensive, and meet the criteria on prospective and retrospective basis. All the information which was collected from the patients was included in the observation tables with different parameters like how long is the patient suffering with diabetes, hypertension and other parameters like age, sex, serum creatinine, proteinuria, present and past medication history and other complications that the patient has been suffering with conditions like cardiovascular complications, diabetic retinopathy, diabetic neuropathy, renal transplantation etc. In observational study of both type 1 and 2 diabetes we found that serum creatinine was increased irrespective of antihypertensive treatment. In our study we found that the proportion of proteinuria levels in type 1 diabetes was almost equal where as in type 2 diabetes the proteinuria levels have been very well controlled.

Keywords: ACE inhibitors, anti-hypertensives, diabetic nephropathy, type 1 and 2 diabetes.

INTRODUCTION

Diabetic Nephropathy (DN) is typically defined by macroalbuminuria that is, a urinary albumin excretion of more than 300 mg in a 24-hour collection or macroalbuminuria and abnormal renal function as represented by an abnormality in serum creatinine, calculated creatinine clearance, or glomerular filtration rate (GFR). Clinically, diabetic nephropathy is characterized by a progressive increase in proteinuria and decline in GFR, hypertension, and a high risk of cardiovascular morbidity and mortality^{1,2}.

Table 1: Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min)
1	Kidney damage with normal or raised GFR	≥ 90
2	Kidney damage with mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	<15

Treatment**Pharmacological treatment**

1. Administration an ACE inhibitor or ARB first line treatment
2. Other anti-hypertensive as second and third line of treatment
3. Dyslipidemia should also be prevented

Either ACE or ARB should be used to reduce albuminuria and the associated decline in GFR that accompanies it in individual's type 1 & type 2 diabetes. Although the direct comparison of ace inhibitors and ARB are lacking, most experts believe that the 2 classes of drugs are equivalent in patients with diabetes. ARB s can use as alternative in patients who developed ACE inhibitor associated cough or angioedema. After 2-3 months of therapy in patients with microalbuminuria, the drug dose is increased until the maximum tolerated dose is reached. Recent studies don't show benefit of intervention prior to onset of microalbuminuria. The combination of an ACE inhibitor and ARB is not recommended and appears to be detrimental. If use of either ace or ARB inhibitors are not possible are BP are not controlled, then, diuretics, calcium channel blockers or beta blockers should be used. These salutary effects are mediated by reducing intra glomerular pressure and inhibition of angiotensin driven sclerosing pathways, in part through inhibition of TGF-beta-mediate pathways^{3,4,5}.

MATERIALS AND METHODS**Study Design**

This is a Prospective and Retrospective study.

Study Area

This study is carried out at two centres.

Centre 1:- Global Hospitals, Lakdikapool, Hyderabad, Telangana, India.

Study population

All the diabetic nephropathy patients fulfilling the inclusion and exclusion criteria will be enrolled in the study from September 2016 to February 2017.

Sample size

The sample size selected is 49 patients, considering maximum 3 follow-up required for each patient. All the diabetic nephropathy patients presenting in our hospitals are outpatient and fulfilling the following inclusion and exclusion criteria after taking written consent will be enrolled in the study (From September 2016 to February 2017).

Patient Selection**Inclusion Criteria**

- ✓ Male and female above 40 years of age.
- ✓ Patients who have been conformed with diabetic nephropathy and on antihypertensive therapy.
- ✓ Patients who meet all the criteria of the study like all the lab values required for the study.

Exclusive Criteria

- ✓ Pregnant or lactating female.
- ✓ Age below 40 years.
- ✓ Renal transplant patients.
- ✓ Patients who are stage 4 or stage 5 of the kidney damage.
- ✓ Patients who are on dialysis.
- ✓ Other types of kidney diseases unrelated to diabetes or high blood pressure can also cause protein to leak into the urine examples ; trauma, toxin, infections, immune system disorder.

Follow up

Laboratory parameters (serum creatinine, CUE) will be assessed at a minimum interval of 15 days, 1 month, and 3 months' time period interval during the next visit of the patients to OPD.

Designing a data collection form**Source of data**

- ✓ Data collection form
- ✓ Treatment chart (present complaints, doctors notes, medication chart)
- ✓ Direct patient interview

Collection of Data

- ✓ Patient's demographics details.
- ✓ Co-morbid conditions.
- ✓ Post medical and medication history.
- ✓ Habituations and addictions.
- ✓ Present medication.

Efficacy and Safety Evaluation

- ✓ Ethical committee approval has been obtained from Institutional ethical committee.
- ✓ Written informed consent was obtained from all the patients before enrollment into the study.
- ✓ Patients visit to the clinical centre were scheduled at screening.

Statistical methods and Data analysis

The statistical data was analyzed using the following formula and results are denoted by the percentage which is used for the comparison studies.

The formula used for the calculation is

$$\text{Percentage of patients or drug} = \frac{\text{No. of patients in each class or drug}}{\text{Total no. of patients}} \times 100.$$

RESULTS

This prospective and retrospective study was conducted after the protocol and the informed consent form (ICF) were reviewed and approved by the Institutional Review Board. The detail procedure followed in this study has been described in the approved protocol "Efficacy of antihypertensives in prolonging diabetic nephropathy". The purpose of the study, details of the procedure involved in the study were lucidly explained to the patients in the vernacular language and version one of the informed consent form, formal written consent was obtained from all the patients they were enrolled into the study.

A total of 49 patients were enrolled into the study based who meet the inclusion and exclusion criteria who are further divided into type 1 and type 2 diabetes. Type 1 diabetes patients are placed in observation 1 and type 2 diabetes patients are placed in observation 2 respectively.

Observation 1:

S.NO	DIABETES TYPE	GENDER	DIABETES SINCE	HYPERTENSION SINCE	ANTI HYPERTENSIVE CLASS	SERUM CREATININE			AVERAGE SERUM CREATININE			PROTEINURIA			AVERAGE PROTIENURIA
						V1	V2	V3				V1	V2	V3	
Pt no.1	Type1	F	8-15 Yrs	8-15 Yrs	β -blocker	2.3	2.2	2.8	2.4	++	+++	+++			3
Pt no.2	Type1	F	over 15 Yrs	over 15 Yrs	β -blocker	1.9	1.9	2	1.9	++	+	+			1.3
Pt no.3	Type1	M	3-8 Yrs	3-8 Yrs	β -blocker, ACE	1	1.4	1.6	1.3	+	+	++			1.3
Pt no.4	Type1	M	8-15 Yrs	8-15 Yrs	Ca ⁺² , β -blocker	3.4	3.8	4	3.7	+	+	+			1
Pt no.5	Type1	F	8-15 Yrs	3-8 Yrs	Ca ⁺² , β -blocker	2.4	2.8	3	2.7	++	++	+++			2.3
Pt no.6	Type1	F	over 15 Yrs	over 15 Yrs	Ca ⁺²	1.6	2.5	3	2.4	+	++	++			1.7
Pt no.7	Type1	M	8-15 Yrs	8-15 Yrs	Ca ⁺²	2.8	2.5	3	2.8	+++	+	+			1.7
Pt no.8	Type1	F	3-8 Yrs	3-8 Yrs	Ca ⁺²	1.7	1.8	2.3	1.9	++	++	+++			2.3
Pt no.9	Type1	F	over 15 Yrs	over 15 Yrs	β -blocker, ACE	2.6	1.3	1.1	1.7	+	+	+			1
Pt no.10	Type1	M	over 15 Yrs	over 15 Yrs	β -blocker, ACE	1.2	1.2	1	1.1	+	+	+			1
Pt no.11	Type1	F	8-15 Yrs	3-8 Yrs	β -blocker, ACE	4.7	4.9	3.4	4.3	+	++	++			1.7

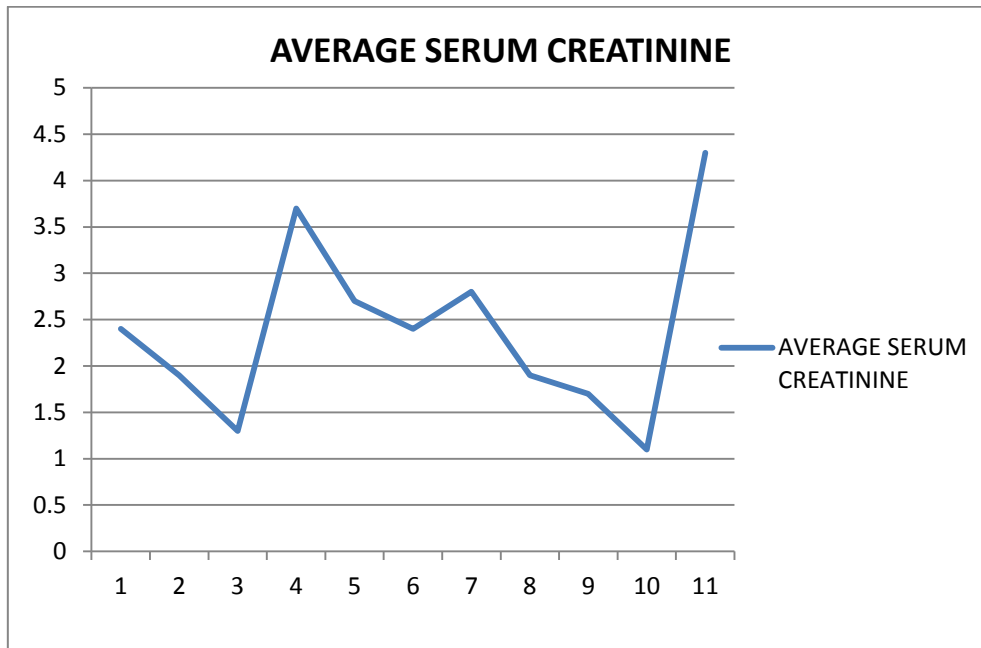


Fig. 1: Type 1 diabetes

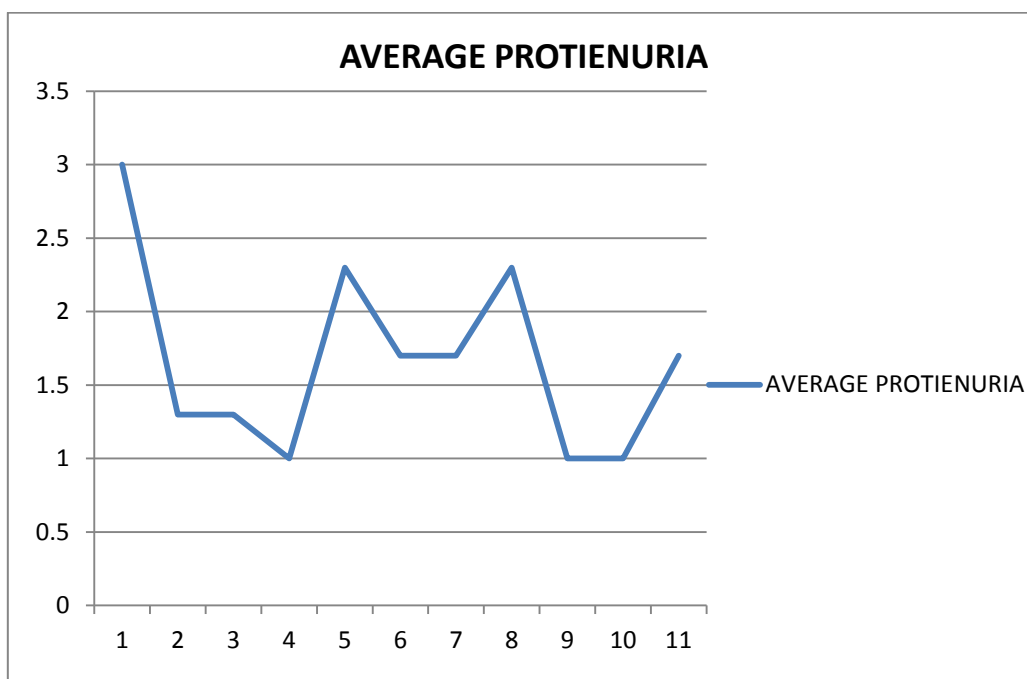


Fig. 2: Type 1 diabetes

Observation 2:

S.NO	DIABETES TYPE	GENDER	DIABETES SINCE	HYPERTENSION SINCE	ANTI HYPERTENSIVE CLASS	SERUM CREATININE			AVERAGE SERUM CREATININE	PROTIENURIA			AVERAGE PROTIENURIA
						V1	V2	V3		V1	V2	V3	
Pt no.1	Type 2	F	8-15 Yrs	8-15 Yrs	Ca ⁺² , β-blocker	2.2	2.5	1.9	2.2	+	+	++	1.3
Pt no.2	Type 2	F	8-15 Yrs	8-15 Yrs	Ca ⁺² , β-blocker	3.8	3.5	3.7	3.7	++	++	++	2
Pt no.3	Type 2	M	3-8 Yrs	3-8 Yrs	Ca ⁺² , β-blocker	2.4	1.2	1.4	1.7	++	+	++	1.7
Pt no.4	Type 2	F	8-15 Yrs	8-15 Yrs	Ca ⁺² , β-blocker	1.6	1.8	5.3	2.9	+++	++	++	2.3
Pt no.5	Type 2	M	over 15 Yrs	8-15 Yrs	Ca ⁺² , β-blocker	4.1	4.2	4	4.1	+++	++++	++++	4
Pt no.6	Type 2	M	over 15 Yrs	over 15 Yrs	Ca ⁺² , β-blocker	1.5	1.7	1.9	1.7	+	+	++	1.3
Pt no.7	Type 2	M	over 15 Yrs	3-8 Yrs	Ca ⁺² , β-blocker	3	4.2	4.8	4	++	++	++	2
Pt no.8	Type 2	M	3-8yrs	8-15yrs	Ca ⁺² , β-blocker	2.9	3.2	3.5	3.2	++	++	++	2
Pt no.9	Type 2	M	3-8 Yrs	3-8 Yrs	Ca ⁺² , β-blocker	1.6	1	1.5	1.4	+++	+	+	1.7
Pt no.10	Type 2	F	over 15 Yrs	over 15 Yrs	α-blocker,β-blocker	1.4	1.2	2.1	1.6	+	+	+	1
Pt no.11	Type 2	M	over 15 Yrs	1-3 Yrs	β+α-blocker	2	2.6	2.8	2.5	+++	+	+	1.7
Pt no.12	Type 2	M	over 15 Yrs	over 15 Yrs	α-blocker,β-blocker	1.1	1	1.4	1.2	+	+	+	1
Pt no.13	Type 2	M	8-15 Yrs	over 15 Yrs	β+α-blocker	2.6	2.3	2.6	2.5	+	+	+	1
Pt no.14	Type 2	M	8-15 Yrs	3-8 Yrs	β+α-blocker	2.6	2.5	2.8	2.6	++	+	+	1.3
Pt no.15	Type 2	M	8-15 Yrs	3-8 Yrs	β+α-blocker	3.2	3	4	3.4	+	+	+	1
Pt no.16	Type 2	M	over 15 Yrs	over 15 Yrs	β+α-blocker	2.6	2.3	3.4	2.8	+	++	+++	2
Pt no.17	Type 2	M	over 15 Yrs	8-15 Yrs	ARB + Ca ⁺²	2.9	3.4	3.2	3.2	++	++	+	1.7
Pt no.18	Type 2	F	over 15 Yrs	8-15 Yrs	ARB + Ca ⁺²	1.9	1.6	1.6	1.7	+	+	+	1
Pt no.19	Type 2	M	8-15 Yrs	3-8yrs	ARB	0.9	0.7	0.9	0.8	+	+	++	1.3
Pt no.20	Type 2	M	3-8yrs	3-8yrs	ARB	1.7	1.5	1.5	1.6	+	+	+	1
Pt no.21	Type 2	F	8-15 Yrs	8-15 Yrs	ARB	1	1.5	2	1.5	++	+++	++	2.3
Pt no.22	Type 2	M	8-15 Yrs	1-3 Yrs	ARB	2.3	2.5	3	2.6	++	+++	++++	3
Pt no.23	Type 2	F	8-15 Yrs	8-15 Yrs	β+α-blocker, Ca ⁺²	1.9	2.3	2.8	2.3	+	+	+	1
Pt no.24	Type 2	M	8-15 Yrs	8-15 Yrs	ARB	1	1.2	1	1.1	+	++	++++	2.3
Pt no.25	Type 2	F	8-15 Yrs	8-15 Yrs	Ca ⁺²	1.6	1.8	2	1.8	++	+	+	1.3
Pt no.26	Type 2	M	over 15 Yrs	over 15 Yrs	Ca ⁺²	1.4	1.7	1.5	1.5	+	+	+	1
Pt no.27	Type 2	M	3-8 Yrs	3-8 Yrs	Ca ⁺²	1.5	1.3	1.4	1.4	++++	++++	++++	4
Pt no.28	Type 2	F	over 15 Yrs	8-15 Yrs	Ca ⁺²	2.3	3	1.5	2.3	+	+	++	1.3
Pt no.29	Type 2	M	over 15 Yrs	3-8 Yrs	Ca ⁺²	2.3	2.8	3	2.7	+++	++	++	2.3
Pt no.30	Type 2	F	3-8 Yrs	3-8 Yrs	β-blocker	2.1	2.5	2.9	2.5	+	+	+	1
Pt no.31	Type 2	M	over 15 Yrs	over 15 Yrs	Ca ⁺²	1.3	1.2	1.3	1.3	+++	++++	++++	3.7
Pt no.32	Type 2	F	8-15 Yrs	8-15 Yrs	Ca ⁺²	1	1.5	2	1.5	++	+++	++	2.3
Pt no.33	Type 2	M	8-15 Yrs	8-15 Yrs	β-blocker	1.9	2.2	3	2.4	+++	+++	+++	3
Pt no.34	Type 2	F	over 15 Yrs	8-15 Yrs	β-blocker	2.4	3.8	4	3.4	+	++	+++	2
Pt no.35	Type 2	F	8-15 Yrs	8-15 Yrs	β-blocker	2.3	2.9	3.5	2.9	+	+++	++	2
Pt no.36	Type 2	M	3-8 Yrs	3-8 Yrs	β-blocker	2.3	2.4	1.9	2.2	+	+	+	1
Pt no.37	Type 2	M	3-8 Yrs	3-8 Yrs	ACE, β-blocker	1.6	1.4	1.5	1.5	+	+	+	1
Pt no.38	Type 2	M	over 15 Yrs	1-3 Yrs	α-blocker,β-blocker,Ca ⁺²	2.4	2.6	3	2.7	+	++	+++	2

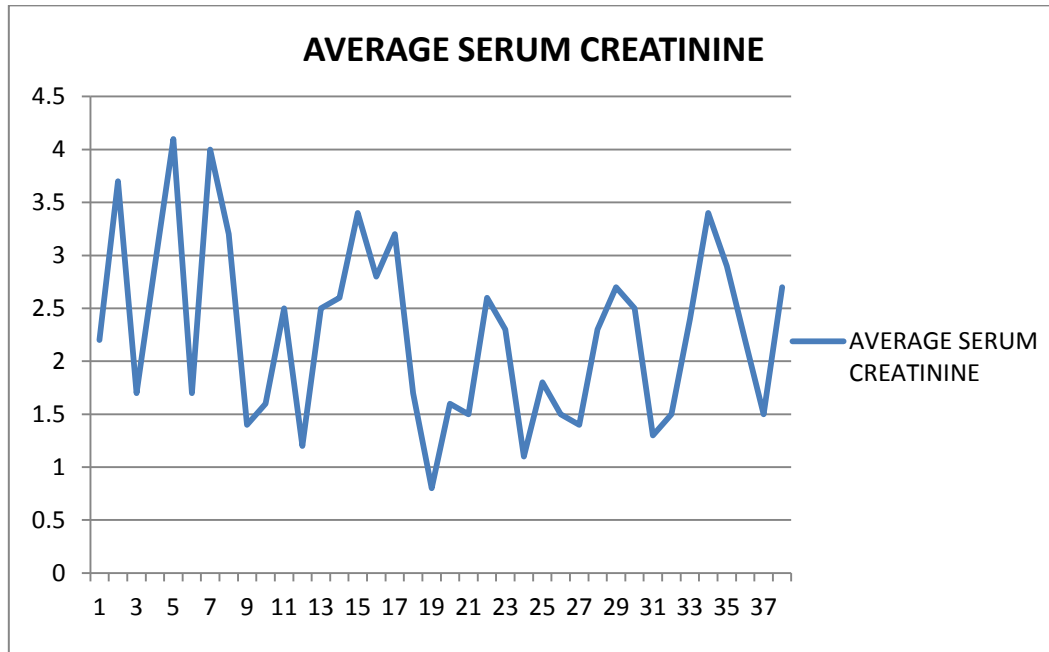


Fig. 3: Type 2 diabetes

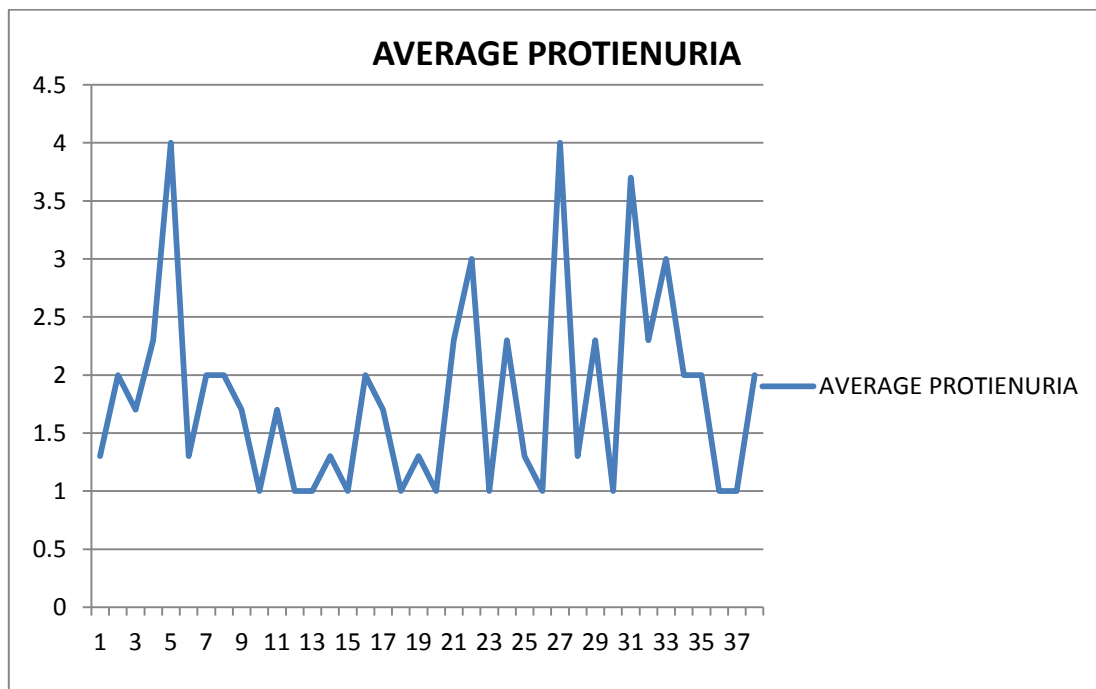


Fig. 4: Type 2 diabetes

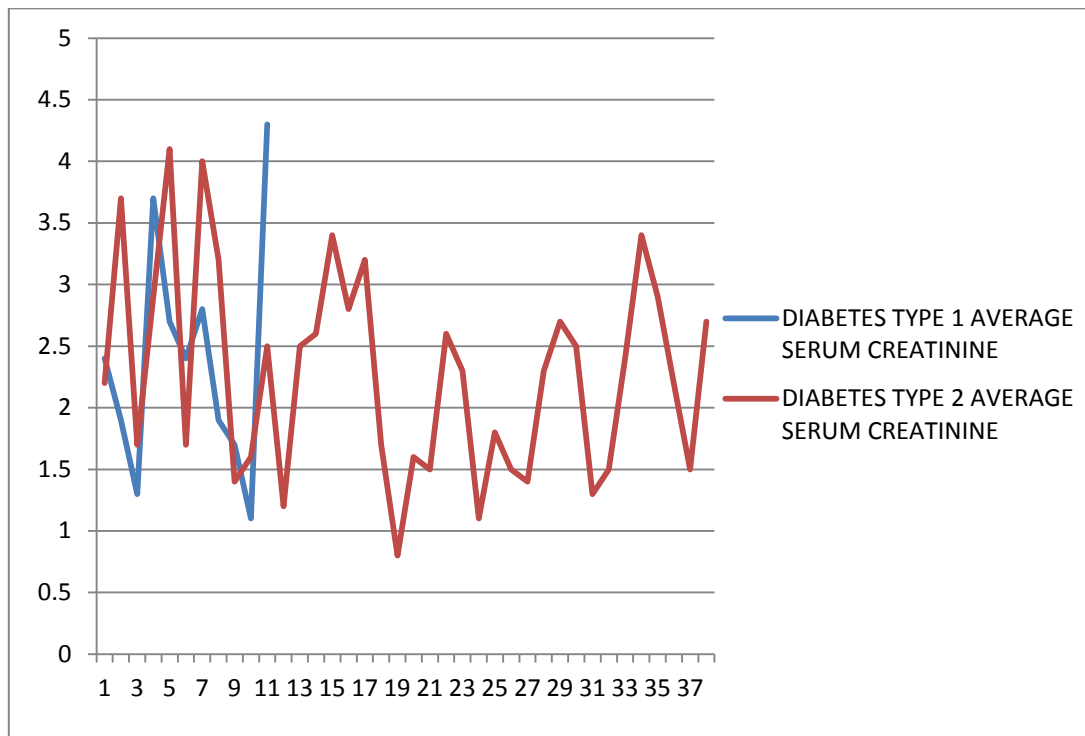


Fig. 5: Comparison serum creatinine of type 1 and type 2 diabetes

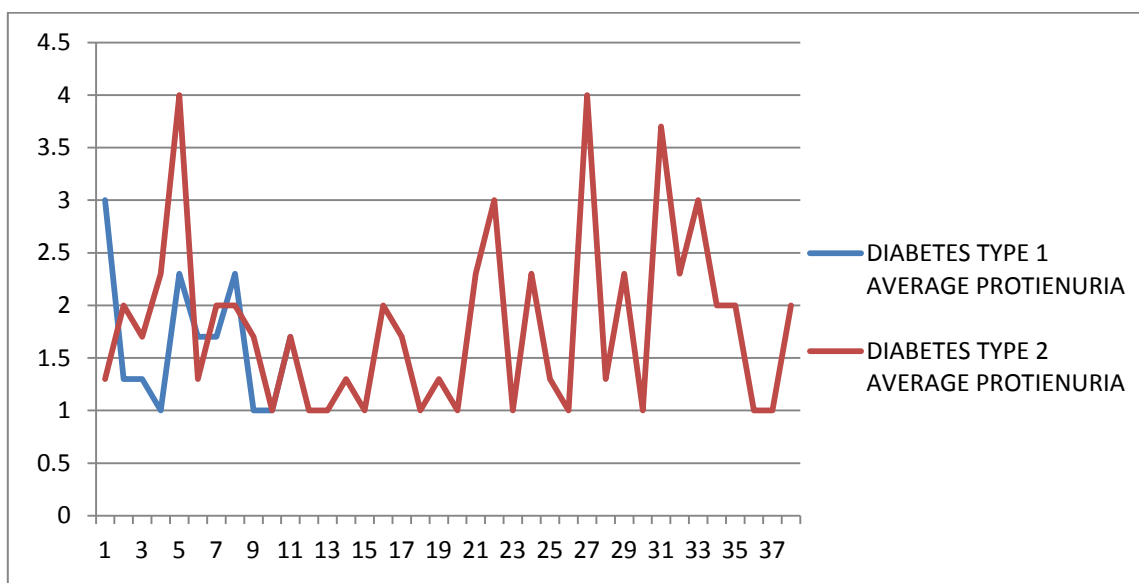


Fig. 6: Comparison proteinuria of type 1 and type 2 diabetes

In the above data shows the comparison of serum creatinine and proteinuria in type 1 and type 2 diabetes.

Proportion of type 1 and type 2 diabetes

A total number of 49 patients were enrolled according to the inclusion and exclusion criteria which include 11 patients of type 1 diabetes and 38 patients of type 2 diabetes.

Table 2: Proportion of type 1 and type 2 diabetes

Total no. of patients	Patients with type 1 diabetes	Patients with type 2 diabetes
49	11	38

All the patients considered into the study were having the history of diabetes of more than 5 years and developing microalbuminuria.

Proportion of Male and Female Patients

Based on the observations 1 and 2 the total number of patients is 49 out of which 32 patients are male and 17 patients are female.

Table 3: Proportion of male and female patients

Total no. of patients	Male	Female
49	32	17

Table 4: Proportion of type 1 diabetes

TYPE 1 Diabetes		
Total no. of patients	Male	Female
11	7	4

The above data tells us the proportion of male and female patients in type 1 diabetes.

Table 5: Proportion of type 2 diabetes

TYPE 2 DIABETES		
Total no. of patients	Male	Female
38	25	13

The above data tells us the proportion of male and female patients in type 2 diabetes.

Table 6: Patients developing cardiovascular complications

TYPE 1 Diabetes		
Total no. of patients	No. of patients with CVD	No. of patients without CVD
11	5	6

Table 7: Patients suffering with cardiovascular diseases in type 2 diabetes

TYPE 2 Diabetes		
Total no of patients	No. of patients with CVD	No. of patients without CVD
38	11	27

Percentage of Results

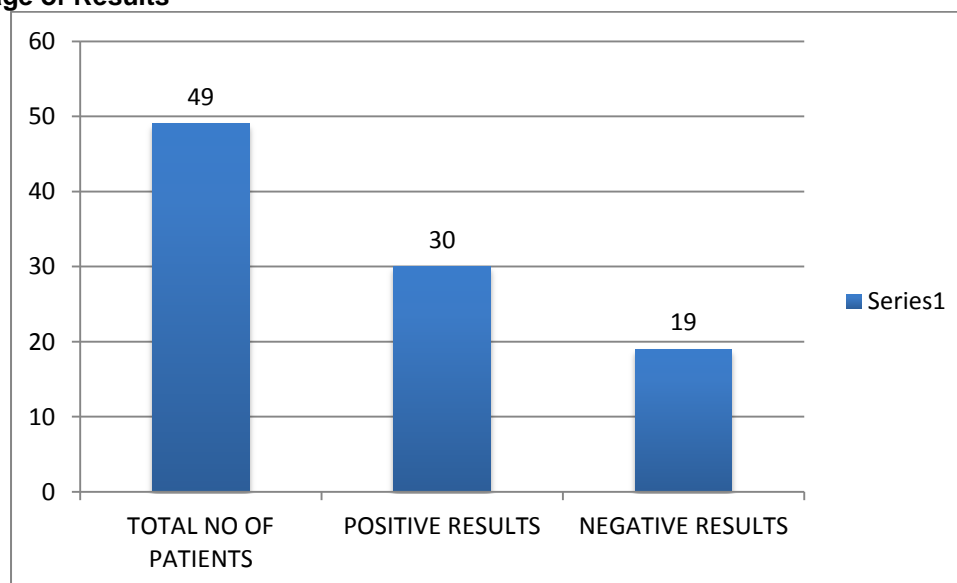


Fig. 7: 49 patients, 30 patients showed the signs of positive results, 19 patients showed the signs of negative results

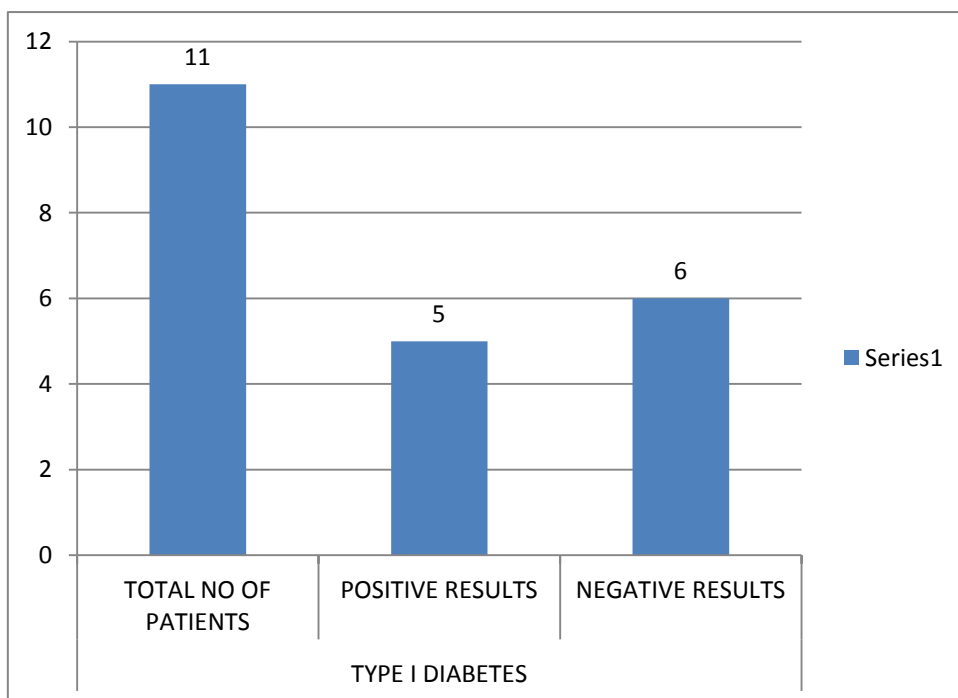


Fig. 8: Patients positive and negative results in type 1 diabetes

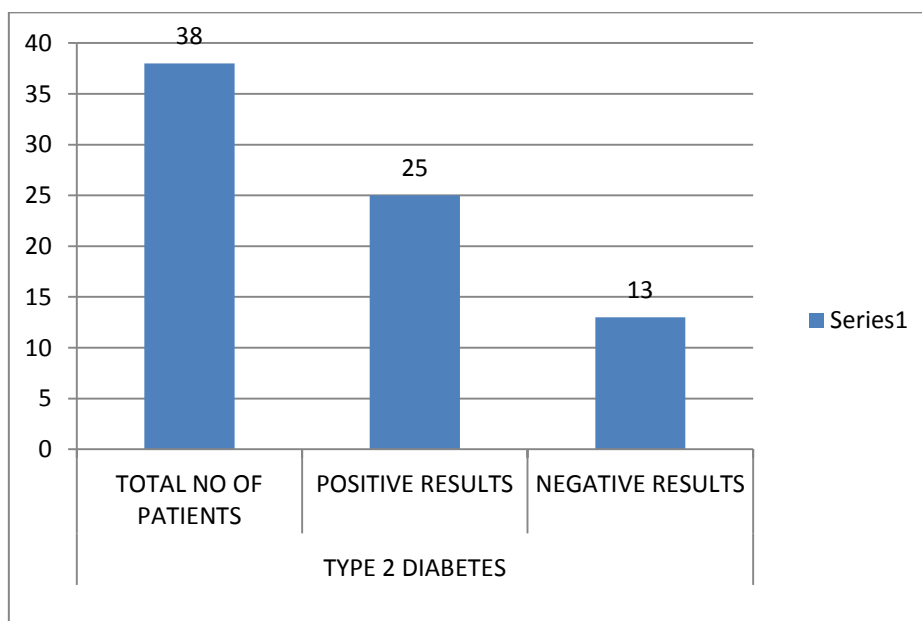


Fig. 9: Patients and the proportion of positive and negative results in type 1 diabetes

Table 8: Anti-hypertensive drugs prescribed in type 1 diabetes patients

TYPE 1 Diabetes				
ANTI HYPERTENSIVE CLASS	β-blockers	Ca ⁺⁺ , β-blockers	Ca ⁺⁺	β, ACE
No. of patients	2	2	3	4

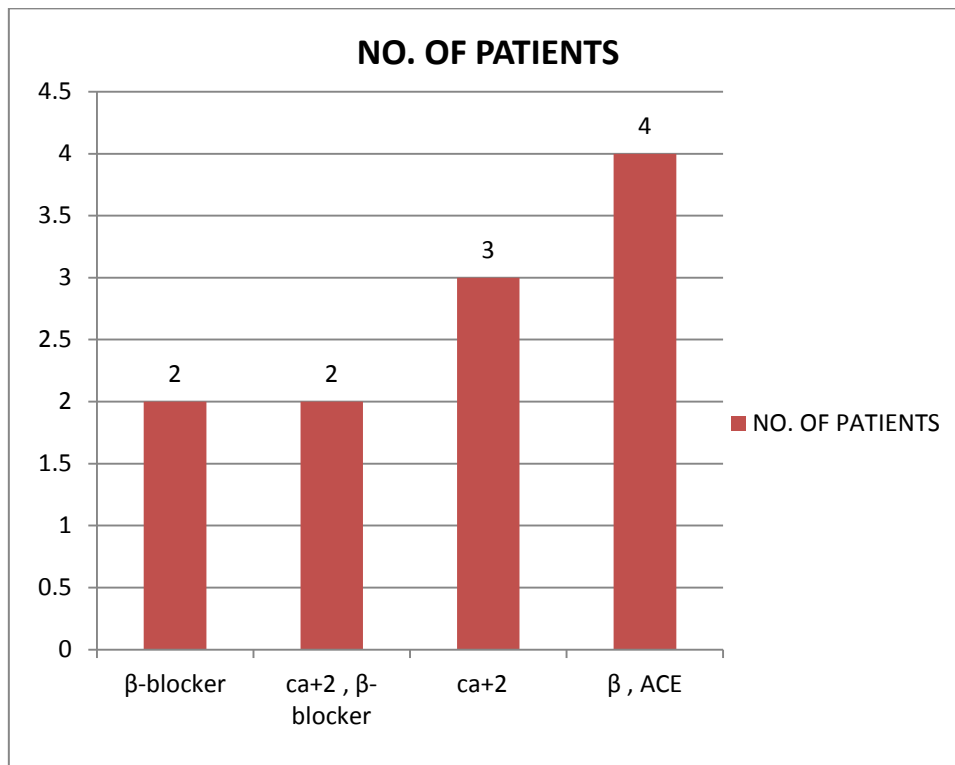


Fig. 10: Antihypertensive drugs prescribed in type 1 diabetes patients

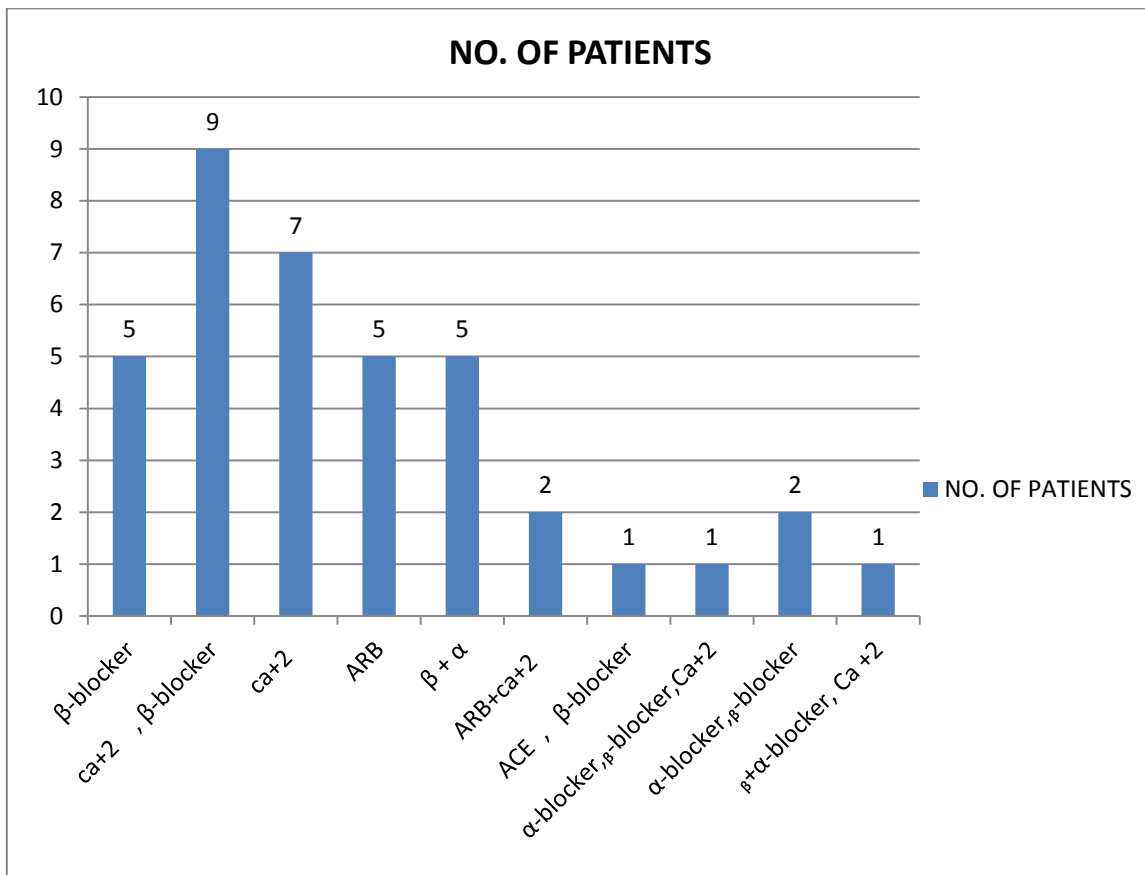


Fig. 11: Anti-hypertensive drugs prescribed in type 2 diabetes patients

The above data shows that the different proportion of antihypertensive and there combinations prescribed in patients with diabetic nephropathy.

Table 9: Efficacy of anti-hypertensives in type 1 diabetes

TYPE 1 Diabetes			
Class of drug	Total no. of patients	Positive results	Negative results
ca ⁺²	3	1	2
ca ⁺² , β-blocker	2	1	1
β-blocker	2	1	1
β, ACE	4	2	2

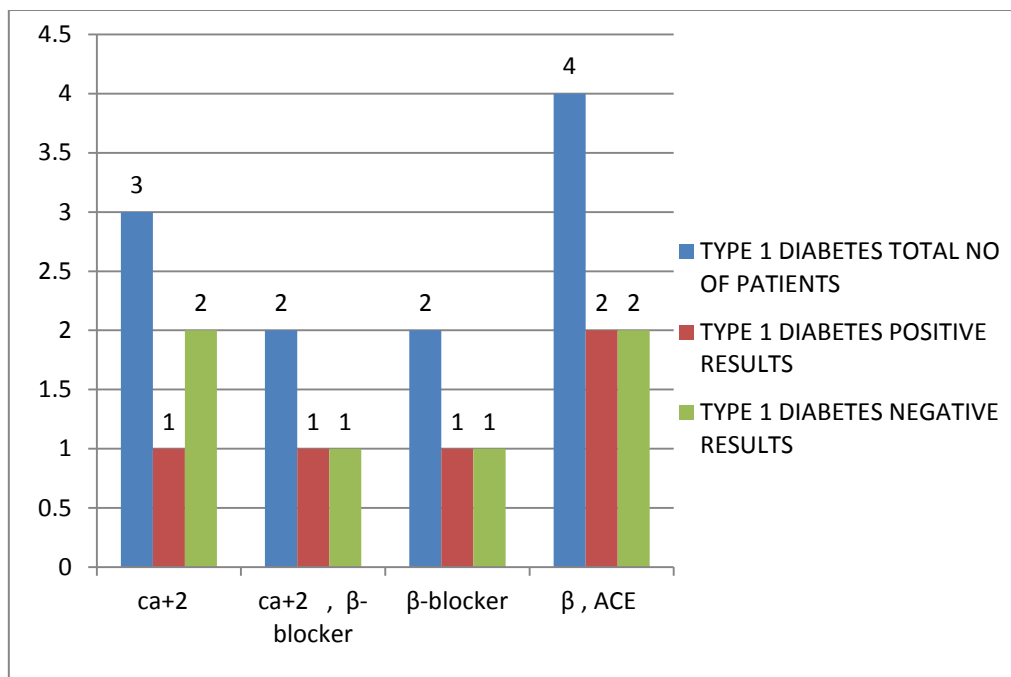


Fig. 12: Efficacy of anti-hypertensives in type 1 diabetes

The above data shows the different antihypertensive classes and the positive and negative results showed by them in type 1 diabetes.

Table 10: Efficacy of anti-hypertensives in type 2 diabetes

TYPE 2 DIABETES			
Class of drug	Total no. of patients	Positive results	Negative results
β + α	5	4	1
ARB + Ca ⁺²	2	2	0
β-blocker	5	3	2
ACE, β	1	1	0
ca ⁺² , β-blocker	9	7	2
ca ⁺²	7	4	3
ARB	5	1	4
β, α, Ca ⁺²	1	0	1
β + α-blocker, Ca ⁺²	1	1	0
α-blocker, β-blocker	2	2	0

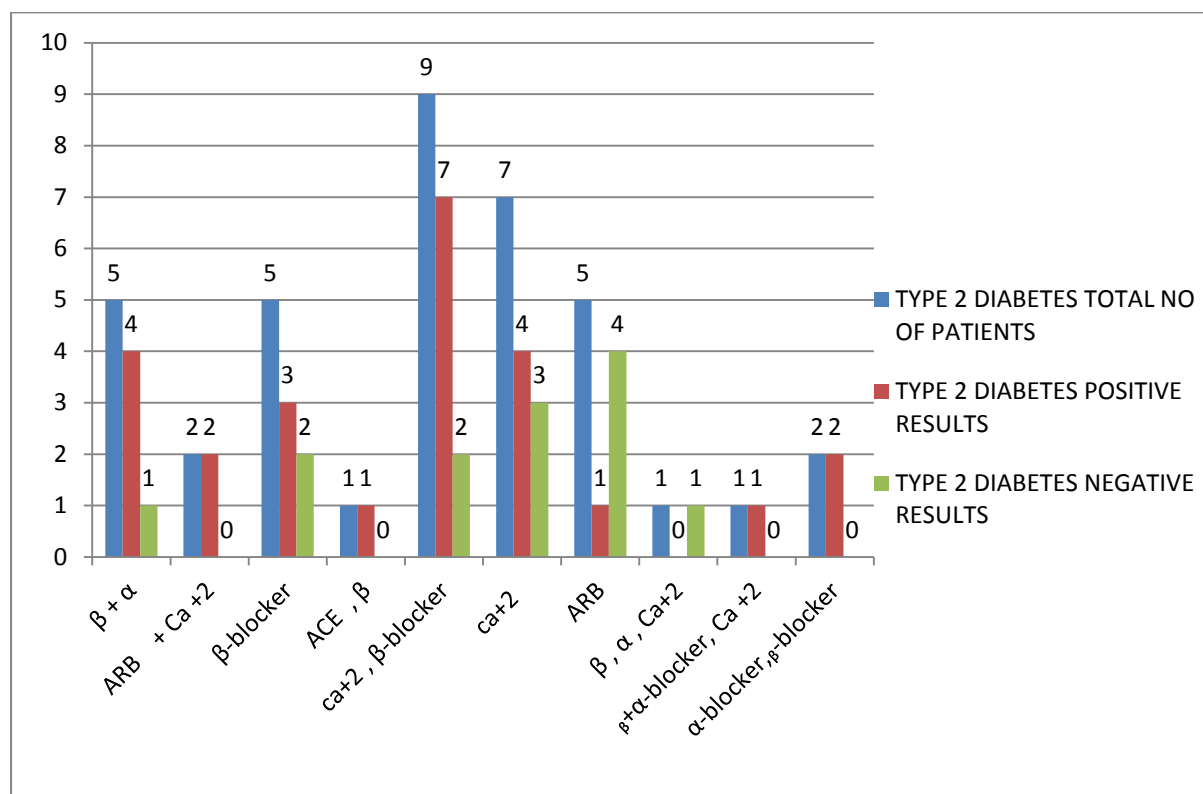


Fig. 13: Efficacy of antihypertensive in type 2 diabetes

The above data shows the different anti-hypertensive classes and the positive and negative results showed by them in type 1 diabetes.

DISCUSSION

The main focus of our study is to know the efficacy of different classes of anti-hypertensive and their combinations in prolonging diabetic nephropathy. The data was collected from the diabetic nephropathy patients who are on antihypertensive, who meet the criteria on prospective and retrospective basis. All the information which was collected from the patients was included in the observation tables 1 and 2 with different parameters like. How long is the patient suffering with diabetes, hypertension and other parameters like age, sex, serum creatinine, proteinuria, present and past medication history and other complications that the patient has been suffering with like cardiovascular diseases, diabetic retinopathy, diabetic neuropathy, renal transplantation etc. In observational study of both type 1 and 2 we found that serum creatinine was increased irrespective of antihypertensive treatment. In our study we found that the proportion of proteinuria levels in type 1 diabetes was almost equal where as in type 2 diabetes the proteinuria levels have been very well controlled.

During our study we found that the proportion of male and female in type 1 diabetes was almost equal, where as in type 2 diabetes the proportion of male was much greater than female patients. Male and the female are having an equal risk factor for developing diabetic nephropathy, even though this relationship is not as strong as in non diabetic renal diseases. The factors involved in this sex specific difference could possibly include lifestyle, diet, kidney and glomerular size, difference in glomerular hemodynamic and direct effect of sex hormones.

The most common complication for the patients suffering with diabetic nephropathy is cardiovascular diseases (CVD). The major cause of mortality in diabetic nephropathy is cardiovascular disease. The underlying pathogenic mechanism that links diabetic nephropathy to a high risk of CVD remains unclear. Coming to the results it has been divided into positive and negative results, results are calculated based on the proteinuria levels during the follow-ups positive result is considered if the proteinuria level either decrease or remain stable, where as negative result are those whose proteinuria levels either increase or fluctuate more than 1st follow up. Considering 49 (100%) patients, 30 patients i.e. 61.2% showed the signs of positive results, 19 patients i.e. 38.8% showed the signs of negative results. Coming to type 1 diabetes out of 11 (100%) patients, 5 patients i.e. 45.5% showed the signs of positive results, 6 patients i.e. 54.5% showed the signs of negative results. In type 2

diabetes out of 38 (100%) patients 25 patients' i.e.65.8% showed the signs of positive results, 13 patients i.e. 34.2% showed the signs of negative results. From the above calculation we can clearly observe that in type 1 diabetes there are negative results irrespective of anti-hypertensive therapy, where as in type 2 diabetes shows a good prolongation on anti-hypertensive treatment.

The anti-hypertensive prescription data shows that the different proportion of antihypertensive and there combinations prescribed in patients with diabetic nephropathy. From the data collected and analyzed we found that the standard therapy for the diabetic nephropathy i.e. first line treatment with ACE and ARB's in type 1 diabetes and ARB's and ACE in type 2 diabetes was not followed in the Indian population. From the study we came to know that the standard first line therapy for diabetic nephropathy was not followed and it mostly depends on patient condition. ACE and ARBs are contraindicated in diabetic nephropathy patients; hence other classes of antihypertensive drugs are preferred.

Considering the individual drug efficacy, in Ca^{+2} channel blockers among 3 patients (100%) 1 patients (33.3%) showed the signs of positive results, 2 (66.7%) patients showed the signs of negative results. In Ca^{+2} , β -blockers among 2 patients (100%) 1 patients (50%) showed the signs of positive results, 1 (50%) patients showed the signs of negative results. In β -blockers among 2 patients (100%) 1 patients (50%) showed the signs of positive results, 1 (50%) patients showed the signs of negative results. Whereas in β -blockers, ACE among 4 patients (100%) 2 patients (50%) showed the signs of positive results, 2 (50%) patients showed the signs of negative results. From the above calculation we found that the efficacy of antihypertensive in prolonging diabetic nephropathy in type 1 diabetes is poor.

Considering the individual efficacy of drugs, $\beta + \alpha$ - blockers among 5 patients (100%) 4 patients (80%) showed the signs of positive results, 1 (20%) patients showed the signs of negative results. In ARB + Ca^{+2} among 2 patients (100%) 2 patients (100%) showed the signs of positive results. In β -blocker among 5 patients (100%) 3 patients (60%) showed the signs of positive results, 2 (40%) patients showed the signs of negative results. In ACE, β -blockers among 1 patient (100%) 1 patient (100%) showed the signs of positive results. In Ca^{+2} , β -blocker among 9 patients (100%) 7 patients (77.8%) showed the signs of positive results, 2 (22.2%) patients showed the signs of negative results. In Ca^{+2} among 7 patients (100%) 4 patients (57.1%) showed the signs of positive results, 3 (42.9%) patients showed the signs of negative results. In ARB among 5 patients (100%) 1 patients (20%) showed the signs of positive results, 4(80%) patients showed the signs of negative results. In β -blocker, α -blocker, Ca^{+2} among 1 patient (100%) 1(100%) patient showed the signs of negative results. In $\beta + \alpha$ -blocker, Ca^{+2} among 1 patient (100%) 1 patient (100%) showed the signs of positive results. In α -blocker, β -blocker among 2 patients (100%) 2 patients (100%) showed the signs of positive results. From the above calculation we found that the efficacy of antihypertensive in prolonging diabetic nephropathy in type 2 diabetes is well. Even though ACE and ARBs are prescribed rarely, we found that in type 2 diabetes among 5 patients who are on ARBs 4 i.e. 80% showed the signs of negative results.

By comparing the above results we found that prolongation of diabetic nephropathy in type 2 diabetes is better when compared with type 1 diabetes by observing the parameter of proteinuria in type 1 and type 2 diabetes.

In our study we found that the use of antihypertensive in diabetic nephropathy has a renal protective effect thus prolonging the disease. This has been already proved. We found that in both type 1 diabetes and type 2 diabetes Ca^{+2} channel blockers and β -blocker either prescribed alone or in combination significantly reduced the proteinuria, thus prolonging diabetic nephropathy.

CONCLUSION

Our study has shown that short term, aggressive antihypertensive treatment includes a progressive reduction in the rate of decline in kidney function, thus postponing renal insufficiency insulin independent patients who have diabetic nephropathy. The present study had showed that the efficacy of antihypertensive in prolonging diabetic nephropathy in type 2 is better when compared to type 1. We found that in both type 1 diabetes and type 2 diabetes Ca^{+2} channel blockers and β -blocker either prescribed alone or in combination significantly reduced the proteinuria, thus prolonging diabetic nephropathy.

FUTURE DIRECTIONS

The major purpose of this study is to improve the quality of life in patients suffering with diabetic nephropathy. From our study we suggest that patients who are on ACE and ARBs are suggested for regular monitoring of complete urine examination and Serum creatinine since ACE and ARBs are contraindicated. We suggest that Ca^{+2} channel blockers and β -blocker either prescribed alone or in combination significantly reduced the proteinuria, so prolonging diabetic nephropathy.

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Conflict of interest

There is no conflict of interest.

ABBREVIATIONS

ACE- Angiotensin Converting Enzyme; ARB- Angiotensin Receptor Blockers; CVD-Cardio Vascular Disease; BP-Blood Pressure; GFR-Glomerular Filtration Rate; GBM-Glomerular Basement Membrane; CUE-Complete Urine Examination, ICF-Informed Consent Form

REFERENCES

1. American Diabetes Association. Last Reviewed: June 1, 2015; Last Edited: June 1, 2015 Diabetes symptoms.
2. Harrison's Principle of Internal Medicine 17 Ed. 2008. Pathophysiology of insulin. Last edited 2008.
3. Afkarian M, Zelnick LR and Hall YN. Clinical manifestations of kidney disease among US adults with diabetes. *Journal of the American Medical Association*. 2016;316(6):602–610.
4. Huo X, Gao L and Guo L. Risk of non-fatal cardiovascular diseases in early-onset versus late-onset type 2 diabetes in China: a cross-sectional study. *The Lancet Diabetes & Endocrinology*. 2016;4(2):115–124.
5. Unnikrishnan R, Rema M and Pradeepa R. Prevalence and risk factors of diabetic nephropathy in an urban South Indian population: the Chennai Urban Rural Epidemiology Study (CURES 45). *Diabetes Care*. 2007;30:2019–24.
6. Agarwal R. Vitamin D, proteinuria, diabetic nephropathy, and progression of CKD. *Clin J Am Soc Nephrol*. 2009;4(9):1523-8.
7. Hans-Henrik Parving, Allanr Andersen, Ulla M Smidt, Eva Hommel, Elisabeth R Mathiesen and Per A Svendsen. Effect Of Antihypertensive Treatment On Kidney Function In Diabetic Nephropathy. *British medical journal*. 1987;294(6585).
8. Parving HH, Andersen AR, Hommel E and Smidt U. Effects of long-term antihypertensive treatment on kidney function in diabetic nephropathy. 1985;7(6 Pt 2):1114-7.
9. Van Buren PN1, Adams-Huet B and Toto RD. Effective antihypertensive strategies for high-risk patients with diabetic nephropathy. 2010;58(8):950-6.
10. Hans-Henrik Parving MDUlla M and SmidtMari-Anne Gall MD. Effective Antihypertensive Treatment Postpones Renal Insufficiency in Diabetic Nephropathy. 1993;22:188-195.
11. Barry M, Brenner MD, Mark E, Cooper MD, Dick de Zeeuw MD and Wil. Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy. *N Engl J Med*. 2001;345:861-869
12. Gudbjörg Andrésdóttir, Majken L, Jensen, Bendix Carstensen, Hans-Henrik Parving, Kasper Rossing and Tine W. Hansen and Peter Rossing. Improved Survival and Renal Prognosis of Patients With Type 2 Diabetes and Nephropathy With Improved Control of Risk Factors. *Diabetes Care*. 2014;37(6):1660-1667.
13. Hans-Henrik Parving MDUlla M and SmidtMari-Anne Gall MD. Effective Antihypertensive Treatment Postpones Renal Insufficiency in Diabetic Nephropathy. 1993;188-195.
14. Giancarlo Viberti FRCP, Carl Erik Mogensen MD and Leif C Groop MD. A Effect of Captopril on Progression to Clinical Proteinuria in Patients with Insulin-Dependent Diabetes Mellitus and Microalbuminuria, *JAMA*. 1994;271(4):275-279.
15. Hermann Haller MD, Sadayoshi IMD, Joseph L Izzo, Jr MD and Andrzej Ja. Effect of Captopril on Progression to Clinical Proteinuria in Patients With Insulin-Dependent Diabetes Mellitus and Microalbuminuria, *N Engl J Med*. 2011;364:907-917.
16. Hans-Henrik Parving, MDD M.Sc, Frederik Persson MD, Julia B. Lewis MD and Edmun. Aliskiren Combined with Losartan in Type 2 Diabetes and Nephropathy. *N Engl J Med*. 2008; 358:2433-2446.
17. Anthony H, Barnett MD, Stephen C, Bain MD, Paul Bouter and Bengt Karlberg M. Angiotensin-Receptor Blockade versus Converting–Enzyme Inhibition in Type 2 Diabetes and Nephropathy. *N Engl J Med*. 2004;351:1952-1961.

18. Agha A, Bashir K and Anwar E. Use of losartan in reducing microalbuminuria in normotensive patients with type-2 diabetes mellitus. 2007;9(2):79-83. PMID: 17899953.
19. Hans-Henrik Parving MD and DM Sc Eva HommelHenrik Post Hansen. Long-Term beneficial effect of ACE inhibitor on diabetic nephropathy in normotensive type 1 diabetic patients. Journal Kidney International. 2001;60.
20. Jennifer L Wilkinson-Berka, Narelle J Gibbs, Mark E Cooper, Sandford L Skinner and Darren J Kelly. Nephrol Dial Transplant. 2001;16(7):1343-1349.