A Controlled Study on Predictors of Type 2 Diabetes in Nodular Diabetic Glomerulosclerosis

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Abstract

Nodular Diabetic Glomerulosclerosis is one of the most familiar diabetic micro vascular complication. A considerable number type 2 diabetic patients are diagnosed regardless of microalbuminuria and with unconcealed and observable nephropathy upon preliminary examination. About 32 to 42% patients with microalbuminuria in type 2 diabetes develops of noticeable nephropathy with in 4 to 5 years, under standard therapy. It is a case control study. Conducted From January to July 2014. Patients visiting the in-patient department of general medicine are selected who has a history of type 2 diabetes mellitus for more than 5-10 years. The diagnosis of diabetic nephropathy was confirmed by 24 hours urine for albumin excretion rate. The study conducted with an aim to estimate the prevalence of 24 hours urinary albumin excretion and to evaluate the etiologic evidence of urinary albumin, creatinine clearance, Serum creatinine, Blood urea. The results show that The mean 24 hour urine albumin level in diabetic nephropathy patients was about 539.65 ± 406.37 and 70.3±34.52 of the control group. In our study it was found that the combine Mean creatinine clearance of males and females in Diabetic nephropathy patients was about 20.52±4.20 and 94.95±8.67 of the control group. serum creatinine clearance also helps in providing the information about how well the kidneys are working. the study concludes thatThe role of albumin excretion is very important to detect diabetic nephropathy which is the leading cause of renal disease. And serum creatinine clearance also helps in providing information about the progression of ESRD.

Keywords: Diabetic nephropathy, microalbuminuria, creatinine, excreation.

Introduction

Diabetic nephropathy or Nodular Diabetic Glomerulosclerosis is one of the most familiar diabetic micro vascular issues. About 20 to 30% range of patients with type one and two diabetes mellitus possesses signs and symptoms of diabetic nephropathy throughout their life time. The frequentness in type 2 diabetes in Indian population has been reported to be around 11%[1].

A considerable number of type 2 diabetic patients are diagnosed with microalbuminuria and with unconcealed and observable nephropathy upon preliminary examination[1].Diabetic nephropathy (D.N) is one of the most conventional micro vascular complication of diabetes, without certain involvement, patients suffering from diabetes with microalbuminuria can advance to ESRD (End stage renal disease) with in 10 to 20 years[1]. In end stage renal disease low albumin level speculates deprived survival[2]. About 32 to 42% of patients with microalbuminuric in type 2 diabetes develops noticeable nephropathy within 4 to 5 years, under standard therapy[3].

D.N patients, mainly those are type 2 diabetes are having high risk possibility for cardio vascular diseases (CVD) were three fold times higher in southern Indian nephropathic volunteers when contrast to their corresponding non-nephropathics, therefore in many patients with type 2 diabetes experience untimely death from CVD and so may not reach End stage renal disease[3].

The American association clarify microalbumuria as secreation of 30-299 mg of albumin in 24-hours collection, having values ≥300 mg is known to be as macroalbuminuria. Albumin storage is a risk element for kidney failure[4]. Watkins et al revealed that IDDM (insulin dependent diabetes mellitus) patients with heavy proteinuria more than (3gm/24hrs) and pronounced renal structural lesions to have worst prognosis[5]. Proteinuria is the unique feature of diabetic nephropathy and is highly predictive of uremia. "Clinical proteinuria"- is a powerful forecaster of future apparent diabetic nephropathy[6]. All patients with persistant proteinuria will develop renal dysfunction[7]. Several centers in Europe have studied the use of albuminuria to foresee and also to ascertain its development[6]. There is a evidence that hypertension plays an critical part in the development of glomerulonephritis. There's a remarkable correlation between hypertension levels and the degree of fall of in glomerular filtration rate[8]. Determining the creatinine clearance is important for evaluating the severity of diabetic kidney disease. Many medication doses are altered for patients with diminished renal function or with the elevated creatinine levels. In various studies of diabetic nephropathy, delay of the progress of nephropathy towards the end stage renal failurehas been found related to foregoing decrease in proteinuria[9].

In recent times meta-analysis proposed that the dietary proteins restriction lowers the occurrence of end stage renal disease or death in patients with non-diabetic nephropathy and slows the development of nephropathy in diabetic individuals[10].

Methodology

This is a case control study done in the in-patient department of princess esra hospital, Hyderabad. From January to July 2014. It is a 1000 bedded teaching hospital, situated in Hyderabad, providing specialized tertiary level health care services to all strata of people.

Patients visiting the in-patient department of general medicine in princess esra hospital were selected for the present study , the patients selected has a history of type 2 diabetes mellitus are on oral hypoglycemic/insulin and are diabetic for than 5-10 years, patients selected had diabetic retinopathy and undergone cataract surgery. Albumin excreation for 24 hours in urine confirms the diagnosis of diabetic nephropathy. All the patients had determined albuminuria on 3 consecutive urine examinations and controlled cases are selected based on their normal albumin excretion profile.

Exclusion criteria: i. patients aged below 30 years ii. patients presenting to emergency department with cardiac emergencies were excluded. iii. Patients who underwent cardiac catheter Surgeries.

A total of 40 participants were enrolled in the study along with the control participants of 40. The participants were enrolled after explaining the study process and taking an informed consent .Blood samples were collected from 40 selected diabetic nephropathy patients on the basis of a history of a retinopathy, persistent albuminuria and hypertension. Of these patients 21 were females and remaining were males 19 are compared with the patients of control group which consist of 22 males and 18 females. Details of the patients like background of type 2 diabetes and other laboratory parameters are recorded in the predesigned Performa which consists Blood Urea, Serum creatinine, Serum Protein, 24 hours urinary albumin, and 24 hours creatinine clearance. Microalbuminuria was describe as 30-300 mg/24 hours and nephropathy values as $\geq$ 300 mmg/24 hrs[11]. Excretion of albuminproteins was detected by enzyme-linked immunosorbent assay[10].All these parameters were investigated, recorded and tabulated. Finally a comparison was made between the diabetic patients and controlled group; later the results were calculated and recorded in terms of means ± standard deviation.

Statistical analysis: Using Microsoft word, Microsoft excels and Epi Info 7 Statistical analysis was done.

Ethical Approval: approval from institutional review board was obtained before the study was initiated.

Aims and Objectives: This case controlled study has been undertaken with the following objectives: i. To study the prevalence of 24 hours urinary albumin excretion and to evaluate the etiologic evidence of urinary albumin, creatinine clearance, Serum creatinine, Blood urea and Serum Proteins in diabetic nephropathy of patients with diabetes mellitus. ii. To determine the mean age and male to female ratio in diabetic nephropathy. iii. To determine the mean creatinine clearance of males and females with diabetic nephropathy.

Results and Discussion

In this study, the mean age of the patients with Diabetic nephropathy was 55.05±8.08 and the mean age of the control group was 47.57±6.67 as shown in table 1.

Table 1
Mean age of patients with diabetic nephropathy and control group

	Mean age of diabetic nephropathy
Diabetic nephropathy patients	55.05 ± 8.08
Control group	47.57 ± 6.67

There are 47.50% of males and 52.50% of females are nephropathic in this study while the control group consist of 55% of males and 45% of females of normal diabetic profile as shown in figure 1.

Table-2
Mean levels of certain clinical parameters in diabetic nephropathy patients

Category	Mean blood urea	Serum creatinine	Serum protein
Normal ranges	40-60 mg/dl	0.5- 1.5 mg/dl	6.0 - 8.0 mg/dl
Diabetic nephropathy patients	108.9 ± 47.3	4.06 ± 1.42	6.78 ± 0.70
Control group	21.05 ± 11.05	0.9 ± 0.22	6.74 ± 0.21

The normal range of blood urea is 40-60mg/dl, but diabetic nephropathy patients exhibits mean blood urea level of about 108.9±47.3 and it was 21.05±11.05 for the control group. The mean serum creatinine level of the diabetic nephropathy patients was about 4.06±1.42 and 0.9±0.22 of the control group as opposed to the normal range of 0.5-1.5mg/dl. In this study, the diabetic nephropathy patients presented with about 6.78±0.70 of the mean serum protein and the control group with about 6.74 ± 0.21 as shown in table 2.

Blood urea levels in diabetic nephropathy patients was above the normal range in 38% of the patients while only 5% of the patients were in the reference range of between 40-60 mg/dl. While almost 90% of the control group were in the normal level as shown in figure 2.
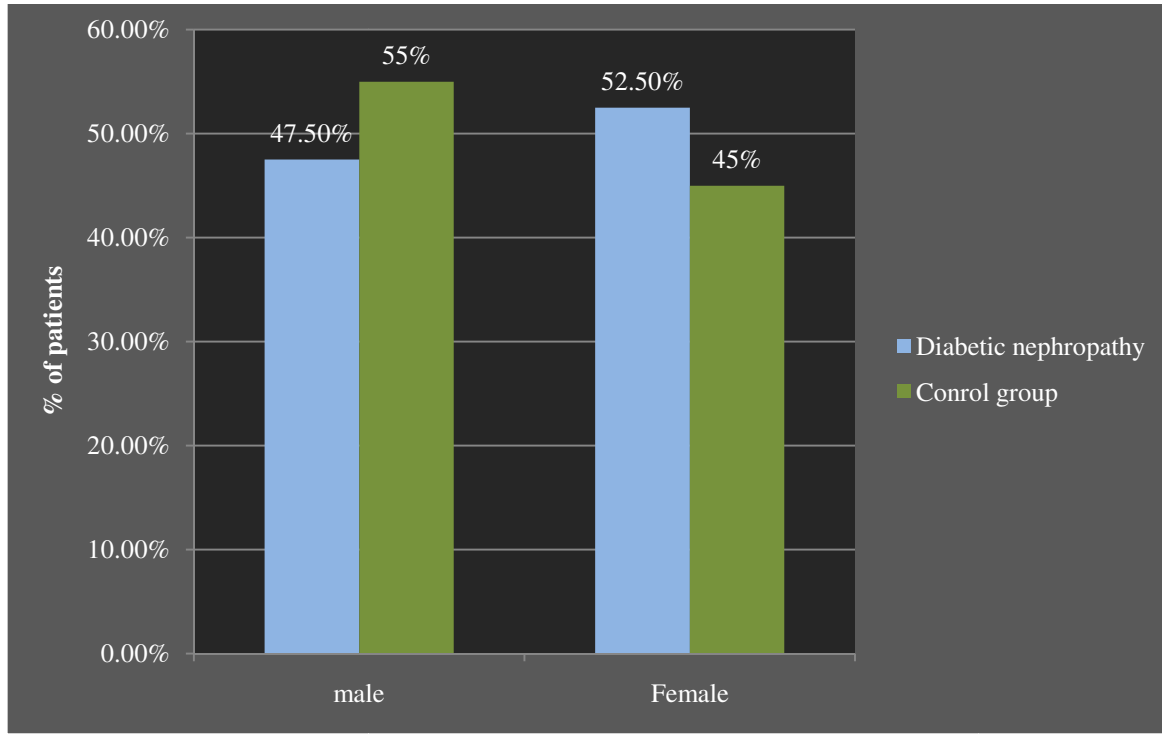
Figure 1
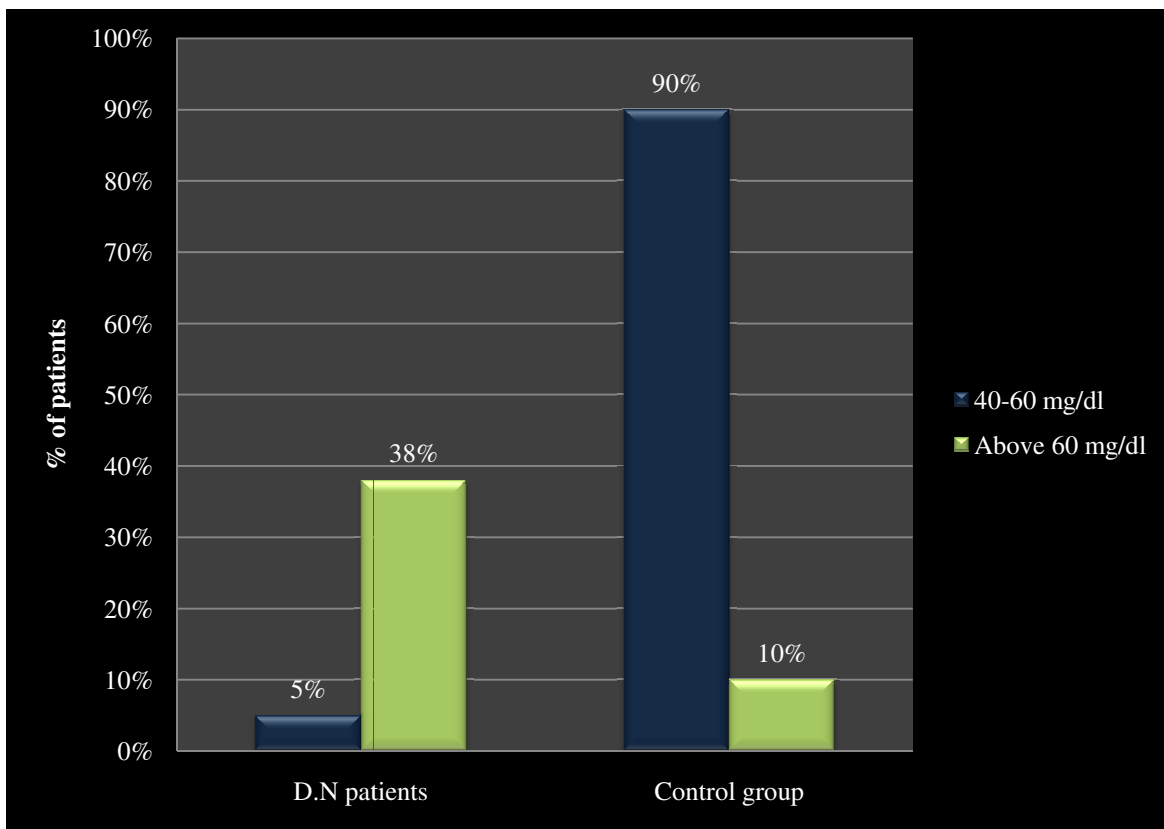**Sex ratio between diabetic nephropathy pateints and control group**

Figure 2
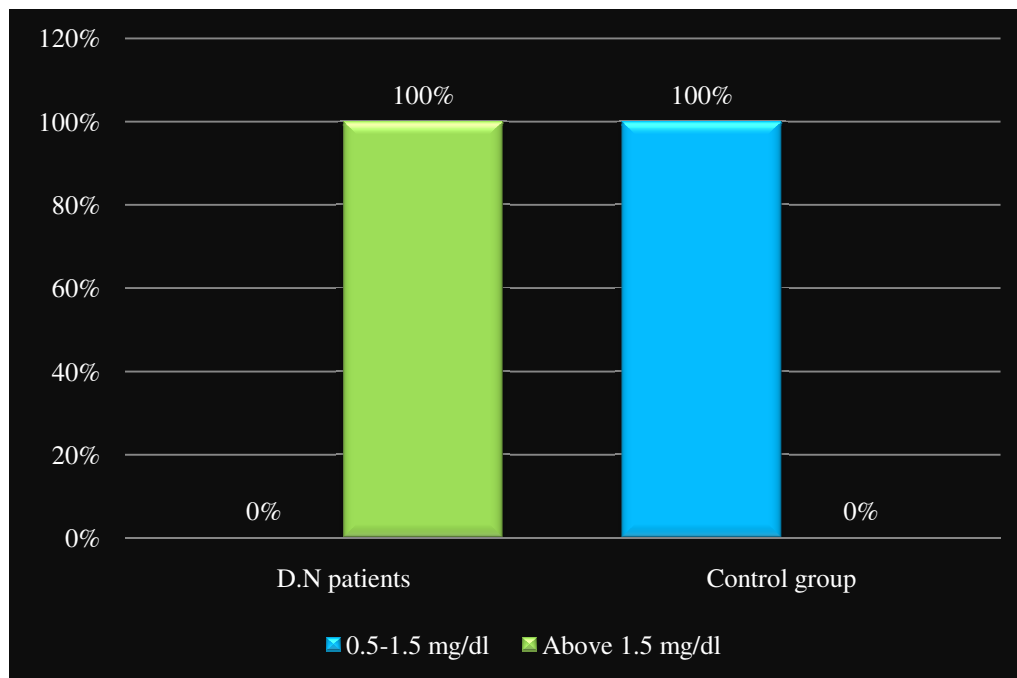**Blood urea levels in diabetic nephropathy patients and control group**

Figure-3
Serum Creatinine levels in Diabetic nephropathy patients vs control group

The creatinine level in D.N patients were above the 1.5mg/dl in 100% of the patients. While it was seen under the normal range in control group.

which comes under the overt nephropathy and macroalbuminuric, as there was only 10% of the patients are microalbuminuric in the current study as shown in figure-4.

Table-3
Mean levels of urine albumin and creatinine clearance

Category	Mean 24 hour urine albumin	Combine Mean creatinine clearance of males and females
Normal ranges	Normal 0-29 mg/24 hrs High microalbuminuria 30-300 V high and nephritic above 300 [12]	
Diabetic nephropathy patients	539.65±406.37	20.52±4.20
Control group	70.3±34.52	94.95±8.67

The mean 24 hour urine albumin level in diabetic nephropathy patients was about 539.65 ± 406.37 and 70.3±34.52 of the control group. In our study it was found that the combine Mean creatinine clearance of males and females in Diabetic nephropathy patients was about 20.52±4.20 and 94.95±8.67 of the control group as shown in table 3. While there are almost 90% of the patients above 300mg/24hr of albumin excreation

Table-4
Mean levels of creatinine clearance in males and females

	Mean creatinine clearance of males	Mean creatinine clearance of females
Normal ranges	97-137 ml/min	88-128 ml/min
Diabetic nephropathy patients	72.31 ± 33.07	68.42 ± 36.4
Control group	96.7 ± 9.18	93.2 ± 9.18

The normal range of Mean creatinine clearance of males is 97-137ml/min, where as in this study the Mean creatinine clearance of males with Diabetic nephropathy was about 72.31 ± 33.07 and 96.7 ± 9.18 of the control group. The normal range of Mean creatinine clearance of females is 88-128 ml/min. However, in this study the Mean creatinine clearance of females with Diabetic nephropathy was 68.42 ± 36.4 and 93.2 ± 9.18 of the control group.

According to the Mean creatinine clearance of males with Diabetic nephropathy shows 73% are below 97 ml/min , 15.7% are in the range of 97-137 ml/min and nearly 26.3% were above 137 ml/min shown in fig 5. while in females it was about 66% ranges below the 97 ml/min, 23.8% are in between 97-137 ml/min and 9.5% were above 137 ml/min as shown in figure-6.
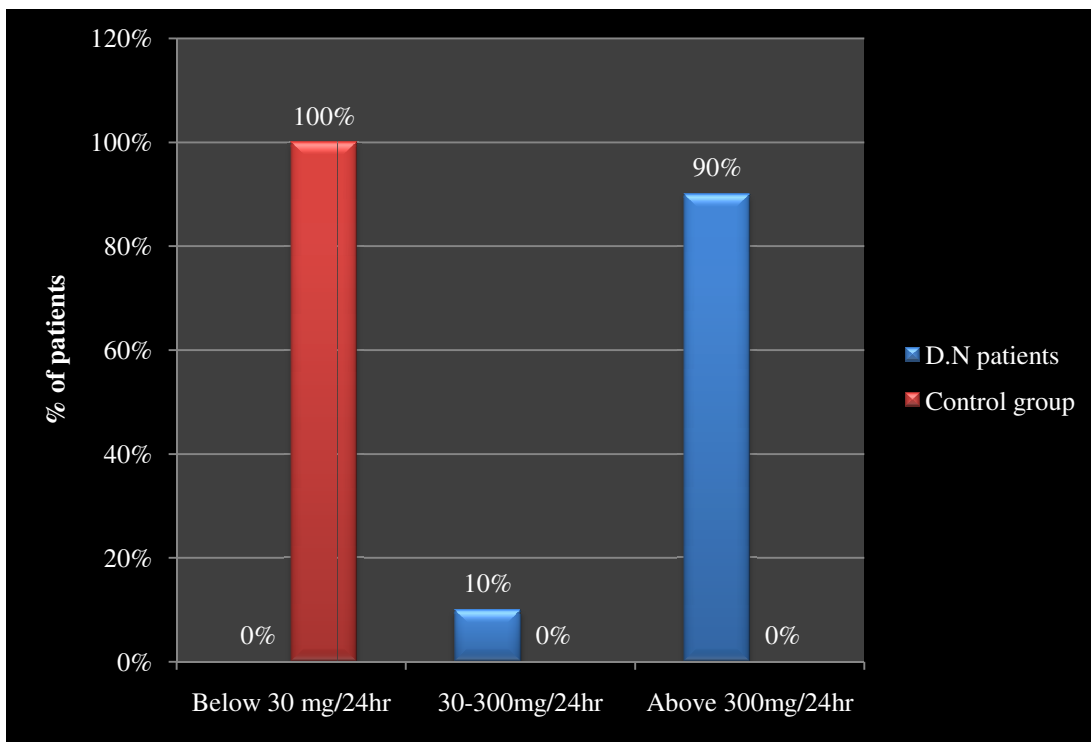
Figure-4
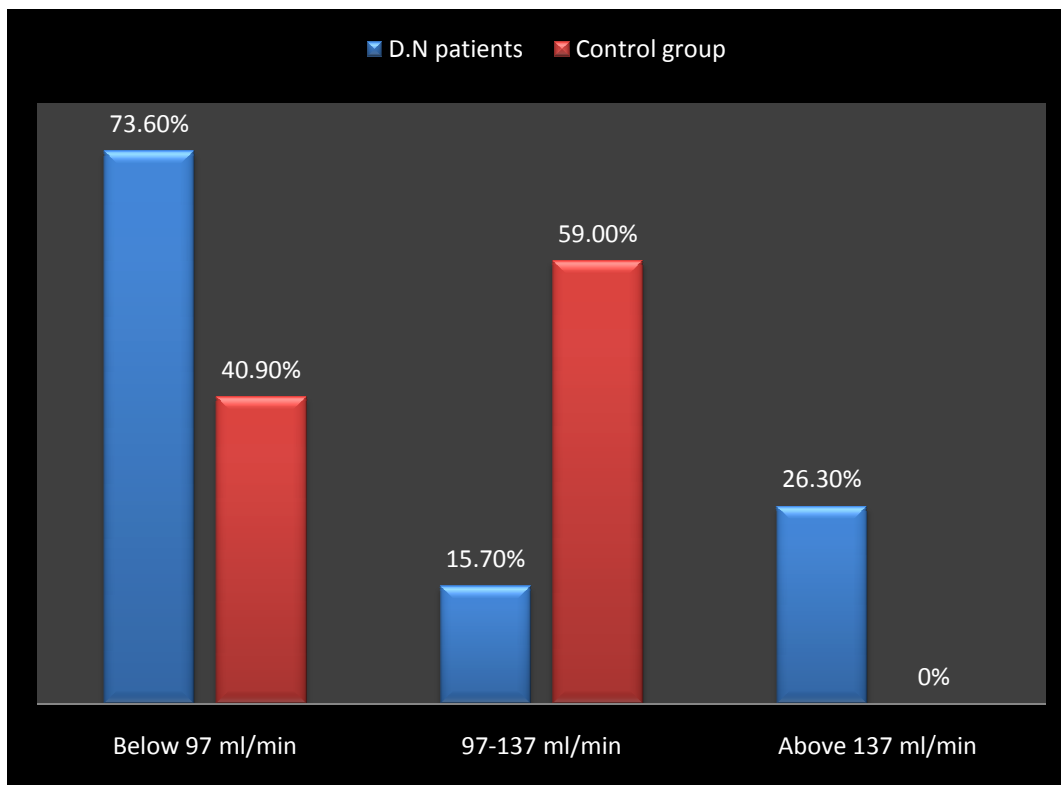**24 hr albumin excreation in Diabetic nephropathy and control group**

Figure-5
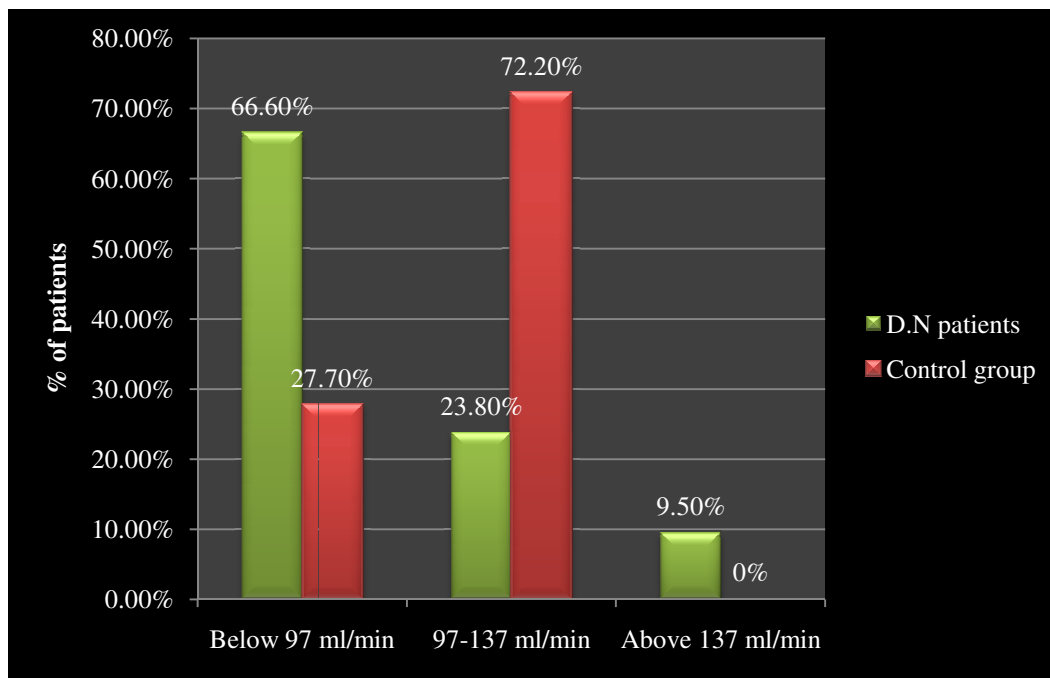**Creatinine clearence of males in D.N and Control group**

Figure-6
Creatinine clearence in females in D.N and control group

Discussion: In the study of *V Viswanathan et al* the male:female ratio in Normoalbuminuria was about 34 / 15, where as it was 34 / 18 in Macroalbuminuria and 30 / 8 in Nephrotic syndrome. The mean age distribution in the *V Viswanathan et al study* was 57 ± 12 in patients with Normoalbuminuria, 56 ± 10 in patients with Macroalbuminuria and 56 ± 9 in patients with Nephrotic syndrome or Albuinuria. The mean urea level in the study of *V Viswanathan et al* in patients with Normoalbuminuria was 21.7 ± 5.6, 27.2 ± 11.3 in Macroalbuminuria and 78 ± 42.1 in Nephrotic syndrome. In our study the mean urea level was 108.9 ± 47.3 in all the three categories.

The mean Creatinine level in patients with Normoalbuminuria was 0.8 ± 0.1, 0.9 ± 0.2 in Macroalbuminuria and 3.1 ± 1.9 in Nephrotic syndrome in the study of *V Viswanathan et al.* however it was same in both Normoalbuminuria and Macroalbuminuria in our study with about 4.06 ± 1.42.

In the study of *V Viswanathan et al* the mean level of Triglyceride for Normoalbuminuria. Macroalbuminuria and Nephrotic syndrome was found to be 153 ± 86, 164 ± 78 and 170 ± 60 respectively. The mean serum albumin level in the study of *V Viswanathan et al* was found to be 4.1 ± 0.4 in Normoalbuminuria, 3.5 ± 0.4 in Macroalbuminuria and 2.8 ± 0.4 in Nephrotic syndrome. In our study it was a constant value of about 6.78 ± 0.70 in all the three categories.

In the study of *V Viswanathan et al* the mean Creatinine clearance was 103.4 ± 25.8 in Normoalbuminuria, 84.1 ± 26.1 in Macroalbuminuria and 32.9 ± 15.6 in Nephrotic syndrome. A

value of about 20.52 ± 4.20 was found to be same for the level of mean Creatinine clearance in all the three categories of our study.

In the study of Frank Pistrosch et al the level of mean creatinine was 84.1 ± 3.3(mmol/l) in Healthy Control subjects as opposed to that of 83.8 ± 4.8 (mmol/l) in patients with type 2 diabetes. In the contemporary study the level of mean creatine was found to be 0.9 ± 0.22 mg/dl in healthy subjects and 4.06 ± 1.42 mg/dl in patients with type 2 diabetes.

the mean urea level in Healthy Control subjects in the study of Frank Pistrosch et al was 6.0±0.3 mmol/l and 5.4 ± 1.5 mmol/l in patients with type 2 diabetes. In a control group it was 21.05 ± 11.05mg/dl and 108.9 ± 47.3mg/dl in patients with type 2 diabetes in our current research.

Conclusion

The role of albumin excretion is very important to detect diabetic nephropathy which is the prime cause of renal diseases. Kidneys remove the complete creatinine from the body, the malformation in kidneys function, results in raised creatinine level in the blood as in turn lead to accumulation of creatinine in body which results in decreased excretion of creatinine through urine. In our research we observe expansive advancement in the interpretation of the risk factor and process of diabetic nephropathy.

References

1. Katherine Tuttle, Md, The Evaluation Of Diabetic Nephropathy: Preventing Complications, *Adv Stud Med*., **5(1a**), S20-S27 **(2005)**

2. Viswanathan V., Snehalatha C., Kumutha R., Jayaraman M. and Ramachandran A., Serum Albumin Levels in Different Stages of Type 2 Diabetic Nephropathy Patients, *Indian J Nephrol,* **14,** 89-92 **(2004)**

3. Management of Diabetes in Chronic Renal Failure, *Indian J Nephrol*, **15(1),** S23-S31 **(2005)**

4. Alan R. Dyer, Philip Greenland Et Al, Evaluation of Measures of Urinary Albumin Excretion in Epidemiologic Studies, *Am J Epidemiol*, **160,** 1122–1131 **(2004)**

5. Peter Rossing, Eva Hommel Et Al, Impact of Arterial Blood Pressure and Albuminuria on the Progression of Diabetic Nephropathy in Iddm Patients, *Diabetes*, **42**, 715-719 **(1993)**

6. Mogensen C.E., Microalbuminuria as a Predictor of Clinical Diabetic Nephropathy, *Kidney International*, **31,** 673—589 **(1987**)

7. Abrahamcohen-Bucay Et Al, Urinarymarkers of Glomerular Injury In Diabetic Nephropathy, *Int J Nep,* 1-11 **(2012)**

8. Mogensen Ce. Blood Pressure Changes And Renal Function Changes In Overt Diabetic Nephropathy, *Hypertension*, **7(11),** 64-11-73 **(1985)**

9. Frank Pistrosch Et Al, Rosiglitazone Improves Glomerular Hyperfiltration, Renal Endothelial Dysfunction, And Microalbuminuria of Incipient Diabetic Nephropathy In Patients, *Diabetes*, **54**, 2206-2211 **(2005)**

10. Henrik P. Hansen Et Al, Effect of Dietary Protein Restriction on Prognosis in Patients with Diabetic Nephropathy, *Kidney International*, **62,** 220–228 **(2002**)

11. Thomas I., Justesen Et Al, Albumin-To-Creatinine Ratio In Random Urine Samples Might Replace 24-H Urine Collections In Screening For Micro- And Macroalbuminuria In Pregnant Woman With Type 1 Diabetes, *Diabetes Care*, **29(4)**, **(2006)**

12. Philip Mcfarlane, Chronic Kidney Disease in Diabetes, *Can J Diabetes*, **37,** S129-136 **(2013**)