American Journal of Advanced Drug Delivery

www.ajadd.co.uk

Original Article

A Case Controlled Study on Clinical Attributes of Patients in Intercapillary Glomerulonephritis

Dr. M. Kaleemullah Khan*[1] and Mohd Nasir Mohiuddin[2]

[1]MD, General Medicine, Associate Professor, Dept. of General medicine, Princess Esra hospital, Deccan College of Medical Sciences, Hyderabad, Andhra Pradesh. India
[2]Pharm-D, intern, Dept. of General Medicine, Princess Esra hospital, Hyderabad, India

Date of Receipt- 27/09/2014
Date of Revision- 13/10/2014
Date of Acceptance- 14/10/2014

Address for Correspondence

Dr. M. kaleemullah khan
MD, General Medicine, Associate Professor, Dept. of General medicine, Princess Esra hospital, Deccan College Of Medical Sciences, Hyderabad, Andhra Pradesh. India.
E-mail: drmkkhan.physcian@yahoo.com

ABSTRACT

Introduction: End stage renal failure eventually develops in 40% of patients with diabetes, the IDDM constitute the single most usual disease leading to inadequacy in adults. Patients with type 2 diabetes had higher HBA1c and FBS together that is distinctly reduced the reactiveness of insulin in contrast to healthy control subjects. On average, death takes place 7years after the start of persistent proteinuria but the scale is wide (2-32) years. Even though morphological bruises advance and nature in glomeruli of those that with diabetes after a few years of metabolic deformities.Chronic hyperglycemia as measured by mean blood glucose or HBA1c has been associated with the development and advancement of micro vascular diabetic complications.

Methodology: This is a case control study done in the in-patient department of general medicine. From January to July 2014. The patients selected has a history of diabetes for more than 3 years and were on hypoglycemic agents/insulin. Diabetic nephropathy was confirmed by elevated levels of blood urea and serum creatinine, which has the level above 6.5 mg/dl. All patients had persistent increase in serum creatinine examinations and controlled cases are selected contingent on their normal creatinine and urea excretion profile.

Results: the mean age of the patients with diabetic nephropathy is 54.43 ± 7.99 while the mean age of patients with control profile of diabetes were 48.37 ± 6.99. There were 22.9%, almost 23% of the patients with diabetic nephropathy are anemic. And the mean FBS levels in diabetic nephropathy in the current study were about180. 85 ± 42.05 and the mean exhibit by control groups 81.4 ± 7.0. While the mean HBA1C range in diabetic nephropathy patients was about 9.96 ± 5.07 and 4.45 ± 0.57 is the mean of the control group. The levels of blood urea, serum creatinine and triglycerides are evidently high,

though which when compared to control group. **Conclusion:** HBA1c and FBS are the important predictors of intercapillary glomerulonephritis or diabetic nephropathy. HBA1c is highly co-related to preceding mean blood glucose. The chief outcome measures which predicts the intercapillary glomerulonephritis or diabetic glomerulosclerosis or diabetic nephropathy are HBA1c, triglycerides, serum creatinine and blood urea nitrogen. Patients with progressed nephropathy showed increased levels of serum triglycerides, which is the important independent clinical attribute.

Keywords: Diabetic nephropathy, HBA1c, Fasting blood sugar, Triglycerides, Serum creatinine.

INTRODUCTION

The clinical syndrome of intercapillary glomerulonephritis is characterized by constant albuminuria analogs that is a continual decrease in the GFR are evaluated systemic BP of all IDDM patients, 35% suffer with this difficulty. Diabetic Nephropathy is the leading cause increased mortality and morbidity in insulin dependent diabetes mellitus (IDDM) patients. Diabetic nephropathy is the principal cause of ESRD (end stage renal disease). On average, death takes place after 7years of start of persistent proteinuria but the scale is wide (2-32) years. Even though morphological bruises advance and nature in glomeruli of those that with diabetes after a few years of metabolic deformities, many diabetics never have major renal disease in a clinical manner even after years of diabetes. On the other side diabetic nephropathy (D.N) that is proteinuria, increases blood pressure and diminished renal function develops in as many as 45% of IDDM insulin dependent diabetes mellitus. It would be of considerable heed to know, actually in the course of diabetes, whether or not a patient was liable for the development of renal disease over the upcoming decade[1, 3]. Renal failure eventually develops in 40% of patients with diabetes, the IDDM constitute the single most usual disease leading to inadequacy in adults[2]. Regardless of this evidently mixed group of diabetic patients and the use of only semi quantitative light microscopy examination, these workers were able to tally hypertension, and renal failure with seriousness of diffused Glomerulosclerosis but were unable to define the significance of other constructional alterations such as glomerular basement membrane thickening or to explain how diffused glomerulonephritis had presented to the renal filure[2]. Renal failure in diabetes ultimately results in abrasions that is the feature of repeated large proteins molecule pressure to enter into the nephrons. The natural past event of nephropathy in IDDM is characterized by a portion of time of clinical quietness that is longer than usual, during which minute practical abnormalities are noticed including GFR (glomerular filtration rate) resulting microalbuminuria a range between 30-300 mg/dl[2].

Early morphological lesions of diabetic nephropathy, such as mesangial expansion and glomerular basement membrane thickenings which mature in basically all Insulin dependent diabetes mellitus patients with a few years after the

prolong metabolic deformity[4]. Mesangial expansion had strong contrary associations that are capillary filtering surface area density. It is hypothesized that mesangial expansion could result in glomerular functional worsening of insulin dependent diabetes mellitus by limiting the glomerular vasculature and its filtering surface[2].

Study from pre centers show that the Mean of microalbuminuria foresees clinical diabetic nephropathy in insulin dependent patients the level of bias of urinary albumin excretion (UAE), that is the level of UAE which is over reached forecasts the development of clinical diabetic nephropathy[4]. Type-2 diabetic patients had higher HBA1c and FBS together that is distinctly reduced insulin sensitivity in contrast to healthy control subjects[5].Chronic hyperglycemia is measured by mean blood glucose or HBA1c has been associated with the development and advancement of micro vascular diabetic complications. A major deciding factor for HBA1c levels is blood sugar levels though it has been found from the population studies in patients that are diabetic that HBA1c is highly co-related to mean blood sugar. There is a considerable variation in HBA1c around the population linear regression line at any given MBG (mean blood glucose) value which is manifested by the evaluation of the relationship between HBA1c and mean blood glucose among individuals within a population[6]. The chief outcome measures which were used to analyze diabetic nephropathy were proteinuria, arterial blood pressure, serum creatinine, HBA1c and creatinine clearance[7].

HBA1C (hemoglobin A1c) incorporate about 3-6% normal human hemoglobin and it is elevated to 6 to 12% in diabetes[8]. A major hallmark feature of diabetes and chronic kidney disease is anemia, which is due to the erythropoietin deficiency and uremic toxicity[9].

Before epithelial to mesenchymal transition the progress of lipotoxicity contributes to the development of diabetic nephropathy in early stages[10]. Thoughts integrated that is the consequences of several studies that indicate and show that the adverse effect of Glycated serum protein on glomerular physiology and biochemistry has produced interest in the exploration of the prospective role Amador modified protein in the development of diabetic nephropathy[11]. Patients with progressed nephropathy showed high levels of serum triglyceride[12]. Sequence of chemical rearrangements, some of the Amadori products are transformed into advance glycoseption end products (AGE) that persistently assemble on long dived protein over time. They accumulate more quickly in the tissues of diabetic patients and has growingly been identified as a major factor in the pathogenesis of diabetic complications because of their highly cross linkage nature[13].

The predominant renal risk markers of diabetic nephropathy on conventional treatment are albuminuria. Renal risk increases with increase in albuminuria reduction in albuminuria is associated with an analogous effect on renal protection, the more the reduction, greater the renal protection[14]. Patients with increased albumin excretion in urine were on the high risk of developing diabetic nephropathy[15].

METHODOLOGY

This is a case control study done in the in-patient Dept. of princess Esra hospital, Hyderabad. From January to July 2014. It is a one thousand bedded teaching hospital, situated in Hyderabad, providing specialized tertiary level health care services to people.

Patients visiting the in-patient department of general medicine in Princess Esra hospital were selected for the current

study, the patients selected has a history of diabetes type 2 for more than 3 years and were on hypoglycemic agents/insulin. The diabetic nephropathy was confirmed by elevated levels of blood urea and serum creatinine, which has the level above 6.5 mg/dl. All patients had persistent increase in serum creatinine examinations and controlled cases are selected on the normal creatinine and urea excretion profile.

Exclusion criteria

1) Patients aged below 30 years 2) patients presenting to the emergency department with cardiac emergencies were excluded. And patients who undergone catheter Surgeries.

A total of 48 participants were enrolled in the study along with the control participants in 45. The patients were enrolled after explaining the study process and taking an informed consent.

Inclusion criteria: 1) patients are included on the basis of a history of a retinopathy. 2) Patients with persistent elevated creatinine levels and hypertension. Of these patients, 24 were females and remaining were males 24 are compared with the patients of the control group which consist of 25 males and 20 females. Details of the patients like history of diabetes and other laboratory parameters were recorded in the predesigned and pretested Performa which consists Blood Urea, CBP (complete blood picture) serum creatinine, Fasting blood sugar, Hba1c, triglycerides, ultrasound examination and fundoscopy. Creatinine was defined as 0.5–1.5 mg/dl and nephropathy as values ≥ 1.5 mg/dl. 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 SPSS statistical analysis are done.

Ethical approval

Approval from IRB (institutional review board) was obtained before the study was initiated.

Aims and objectives

- To mark out the important clinical attributes of type 2 diabetes and to evaluate the causative evidence of CBP, FBS, HBA1C, serum creatinine and blood urea in patients with diabetic nephropathy and diabetes mellitus.
- This case controlled study has been undertaken with the following objectives and also compare with Triglycerides, fundoscopy and ultrasound abdomen to rule out parenchymal changes of the kidneys.
- To determine the mean age and male to female ratio in diabetic nephropathy.

RESULTS

The overall numbers of 83 patients are included in the study, 48 patients are nephropathic and the rest of 45 patients with normal diagnostic profile include in the study.

The mean age of the patients with diabetic nephropathy is 54.43 ± 7.99 while the mean age of patients with control profile of diabetes were 48.37 ± 6.99 as can be seen in table 1.

There were 50% of males and 50% of females are having diabetic nephropathy, as the control group consists of 55.50% of males and 44.40% of females as shown in figure 1.

The prevalence of anemia is 22.9%, almost 23% of the patients with diabetic nephropathy are anemic. As the control group

is having a normal blood profile. Though there may a be a more chance in diabetic nephropathy patients to have a decrease levels of erythropoietin, which results in low production of RBC, even with this feature as a major concerned we have diagnosed 22.9% patients with anemia as shown in table 2.

The normal range of FBS is 70-100 mg/dl, but in early diabetic stage patients have a normal level of FBS 101-126 mg/dl and in patients with established diabetes having the raised FBS level to or more than 126 mg/dl. The mean FBS in patients with diabetic nephropathy in the current study was about180. 85 ± 42.05 and the main exhibit by control group is 81.4 ± 7.0. The mean HBA1c levels in patients with diabetic nephropathy were about 9.96 ± 5.07 and 4.45 ± 0.57is the mean of the control group. As opposed to the normal range of ≤ 5.7%, in pre-diabetics 5.7-6.4% and in diabetic individuals it was equal to or above 6.5% can be seen in table 3.

Patients with diabetic nephropathy in the current study have mostly fallen under the category of established diabetes that is 93.70% of the patients with nephropathy having the fasting blood sugar (FBS) ≥ 126 mg/dl. As almost 100% of the patients in the control group was below the normal range as shown in figure 2.

Almost 99% of the Individuals with diabetic nephropathy having the HBA1C levels above or equal to 6.5% and only 1% is having an HBA1c level in prediabetic that is between 5.7 – 6.4%. While 100% of the patients in the control group are within the range of normal limits that is less than or equal to 5.7% as shown in figure 3.

The normal level of blood urea is 40-60mg/dl, but diabetic nephropathy patient exhibits mean blood urea level of about 112.97 ± 68.19 and it was 22.48 ± 14.49 for the control group. The mean serum creatinine levels of the diabetic nephropathy patients were about 3.97 ± 1.30 and 0.92 ±0. 22 of the control as opposed to the normal range of 0.5-1.5mg/dl. In the current study, the diabetic nephropathy patients presented with about 257.9± 66.1 of the mean triglycerides and the control group with about 153.9 ± 8.5 as shown in table 4.

Blood urea levels in diabetic nephropathy patients were above the borderline in 6.25% of the patients while 93.7% of the patients were above 60 mg/dl. As almost 100% of the control group were in the normal range. The creatinine level in D.N patients was above the 1.5mg/dl in 100% of the patients. While it was seen under the normal range in the control group. But as in the triglycerides it is being fluctuated in the control group too, it was seen that 37.7% of the control group fall under the reference range of ≤ 150 mg/dl and 62.2% comes under the borderline of 150-199 mg/dl While in diabetic nephropathy patients it was shown that 27% comes under the borderline while 72.9% are in the high reference range as shown in table 5.

Under the diagnostic sonography, it was revealed that nearly 63% of the diabetic nephropathy individuals have grade 2 ultrasonographic findings, while 19% are with the grade 3 findings and 14% are with the grade 1 diagnosis, The rest of the4% have the normal ultrasonographic findings as shown in figure 4.

In the evaluation of fundoscopy it is seen that 62.50% of the D.N patients having non-proliferative and 37.50% were having proliferative fundoscopy. While the control group it was revealed that 33.3% are non-proliferative and 66.6% are diagnosed as normal as shown in figure 5.

DISCUSSION

In the study of E. Esmatjes *et al* the age of the patients with diabetic nephropathy 30.7±9.3 years with diabetes duration, whereas it is 54.43 ± 7.99 in our study[17].

The mean hemoglobin values between diabetes type 2 and non diabetic patients with

same renal function in the study of Dousdampanis P, et *al* was 12.5 ± 1.8 and 12.6 ± 1.7 g/dl respectively with no significant differences. In diabetic patients with CKD stage III-IV anemia is more common than in non diabetic patients with similar renal function[9].

However, in our study, 22.9% patients with diabetic nephropathy were anemic and none were in the control group.

The level of creatinine in the study of frankporsch *et al* was 0.95 ± 3.3 in control subjects and 0.94 ± 4.8 in patients with type 2 diabetes. In our study it was 0.92 ± 0.22 in healthy control subjects and 3.97 ± 1.30 in patients with type 2 diabetes.

In the study of frankporsch *et al* the level of urea in healthy control subjects was 16.8 ± 0.3 and 15.1 ± 1.5 in Type 2 diabetic patients. The level of urea in our study in a healthy control subjects was 22.48 ± 14.49 and 112.97 ±68.19 in Type 2 diabetic patients.

The level of Triglycerides in our study was 153.9 ± 8.5 in healthy control subjects and 257.9 ± 66.1 in Type 2 diabetic patients. In the study of frankporsch *et al* it was 61.7 ± 0.8 in healthy control subjects and 69.4 ± 0.9 in Type 2 diabetic patients.

In the study of frankporsch *et al* the HBA1C (%) in healthy control subjects was 5.3 ± 0.3 and 6.7 ± 0.7 in Type 2 diabetic patients. However, it was 4.45 ± 0.57 in healthy control subjects and 9.96 ± 5.07 in patients with type 2 diabetes.

The fasting blood glucose levels in the study of frankporsch *et al*, in healthy control subjects were 88.5 ± 7.2 and 133.8 ± 12.6 in patients with type 2 diabetes. In our study it was 81.4 ± 7.0 and 180.85 ± 42.05 for healthy control subjects and Type 2 diabetic patients respectively.

In a study of Xu Y, Huang J, et *al* describes that during the development of diabetic nephropathy, the progress of lipotoxicity participates in the early stage before EMT epithelial-to-mesenchymal transition. In diabetic nephropathy, a promising therapeutic intervention is the manipulation of lipid metabolism in which our study shows a severe increase in lipid levels, which states that lipotoxicty may be the most important predictor of diabetic nephropathy[10].

In the study of S Hadjadj *et al*, the levels of Serum triglyceride (TG) in patients who progressed in nephropathy were higher than in those who did not [median 1.21 (range 0.41-2.96) *vs* 0.91 (0.31-11.07) mmol/l; p = 0.0037] (12). In a current study were 257.9 ± 66.1 in patients who have progressed nephropathy and 153.9 ± 8.5 in patients who did not show any progress in nephropathy[12].

A target glycated hemoglobin level of 7.0 % or less is recommended in current guidelines for most diabetic patients. In the study of The ADVANCE Collaborative Group *et al* the mean glycated hemoglobin (HBA1c) values were 6.5 in the intensive group and 7.3% in the standard-control group. However, it was 9.96 ± 5.07 in intensive group or D.N group and 4.45 ± 0.57 in the standard-control group[16].

CONCLUSION

Patients with type 2 diabetes had higher HBA1c and FBS together that is distinctly reduced insulin sensitivity in contrast to healthy control subjects and perhaps our state that HBA1c and FBS are the important clinical attributes of diabetic nephropathy. HBA1c is highly co-related to preceding mean blood glucose.

The chief outcome measures which predict the diabetic nephropathy were HBA1c, blood urea nitrogen, serum creatinine and triglycerides. Perhaps there may be also be a major feature of diabetes and chronic kidney disease is anemia, which is majorly due to erythropoietin deficiency and uremic toxicity.

Patients with progressed nephropathy showed high levels of serum triglyceride which is the important independent clinical attribute of complications in patients with diabetic nephropathy.

REFERENCES

1. C. E. Mogensen, And C. K. Christensen. Predicting Diabetic Nephropathy in Insulin-Dependent Patients, *N Engl J Med* 1984; 311:89-93 july 12, 1984 Doi: 10.1056/Nejm198407123110204.
2. S. Michael Mauer, Michael W. Steffes, Eileen N. Ellis, David E. R. Sutherland, David M. Brown, *J. Clin. Invest*. The American Society for Clinical Investigation, Volume 74, October 1984, 1143-1155.
3. Peter Rossing, Eva Hommel *et al*, Impact of Arterial Blood Pressure and Albuminuria on The Progression of Diabetic Nephropathy in Iddm Patients. *Diabetes*, 1993; May Vol. 42:715-719.
4. C. E. Mogensen, Microalbuminuria as A Predictor of Clinical Diabetic Nephropathy. *Kidney International*, Vol. 31(1987), Pp. 673-589.
5. Frank Pistrosch *Et al*, Rosiglitazone Improves Glomerular Hyperfiltration, Renal Endothelial Dysfunction, And Microalbuminuria of Incipient Diabetic Nephropathy in Patients. *Diabetes*, 2005; July Vol. 54: 2206-2211.
6. Robert J. Mccarter, James M. Hempe, Ricardo Gomez, Stuart A. Chalew, Biological Variation In Hba1c Predicts Risk Of Retinopathy And Nephropathy In Type 1 Diabetes. *Diabetes Care*, Volume 27, Number 6, June 2004.Pg 1259-1264.
7. Biesenbach G, Grafinger P, Janko O, Zazgornik J. Nfluence of Cigarette-Smoking on the Progression of Clinical Diabetic Nephropathy in Type 2 Diabetic Patients. *Clinical Nephrology* 1997, 48(3):146-150.
8. Ronald J. Koenig, B.S., Charles M. Peterson *et al,* Hemoglobin Aic as an Indicator of The Degree Of Glucose Intolerance In Diabetes. *Diabetes*, March, 1976.Vol. 25, No. 3, 230-232.
9. Dousdampanis P, Trigka K, Fourtounas C Prevalence Of Anemia In Patients With Type Ii Diabetes And Mild To Moderate Chronic Kidney Disease And The Impact Of Anti-Ras Medications. *Saudi Journal of Kidney Diseases and Transplantation*. 2014, 25(3):552-557.
10. Xu Y, Huang J, Xin W, Chen L, Zhao X, Lv Z, Liu Y, Wan Q. Lipid Accumulation Is Ahead Of Epithelial-To-Mesenchymal Transition And Therapeutic Intervention By Acetyl-Coa Carboxylase 2 Silence In Diabetic Nephropathy. Metabolism: *Clinical and Experimental* 2014, 63(5):716-726.
11. Role of Amadori-Modified Nonenzymati -cally Glycated Serum Proteins in the Pathogenisis of Diabetic Nephropathy. Margo P. Cohen, Fuad N. Ziyadeh. *Journal of American Society of Nephrology*. 1996; 7: 183-190.
12. S Hadjadj, B Duly-Bouhanick. Serum Triglycerides Are A Predictive Factor For The Development And The Progression of Renal And Retinal Complications In Patients With Type 1 Diabetes. Doi: 10.1016/S1262-3636(07) 70088-5.
13. Zenji Makta, Radoff *Et al*, Advanced Glycosylation End Products in Patients with Diabetic Nephropathy. *New England Journal of Medicine*. 1991, Vol 35 (12) 836-842.
14. Di ck De Zeeuw, Giuseppe Remuzzi, Hans-Henrik Parving *Et al* , Proteinuria, A Target For Renoprotection In Patients With Type 2 Diabetic Nephropathy: Lessons From Renaal. *Kidney International,* Vol. 65 (2004), Pp. 2309–2320.

15. J. Vigstrup, C. E. Mogensen. Proliferative Diabetic Retinopathy: At Risk Patients Identified By Early Detection of Microalbuminuria, *Acta Ophthalmologica*, October 1985 Volume 63, Issue 5, Pages 530-534.
16. The Advance Collaborative Group. Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes. *N Engl J Med*. 2008; 358 (12):2560-2572. 2008 doi: 10.1056/ Nejmoa 0802987.
17. E. Esmatjes, F. De Alvaro. Incidence of Diabetic Nephropathy in Type 1 Diabetic Patients in Spain: 'Estudio Diamante'. *Diabetes Research and Clinical Practice*. Volume 57, Issue 1, July 2002, Pages 35–43.

	Mean age of diabetic nephropathy
Diabetic nephropathy patients	54.43 ± 7.99
Control group	48.37 ± 6.69

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

Table 2. Anemia prevalence in diabetic nephropathy patients

	D.N patients	Control group
Anemic	22.9%	0%

Table 3. Mean levels of FBS and HBA1c in Diabetic nephropathy

	Mean fasting blood sugar	HBAIC
Normal ranges	Normal: 70-100 mg/dl Early diabetic : 101-126 mg/dl Established diabetes ≥ 126 mg/dl	Normal : ≤ 5.7% Pre-diabetics : 5.7-6.4% Diabetes ≥ 6.5%
Diabetic nephropathy patients	180.85 ± 42.05	9.96 ± 5.07
Control group	81.4 ± 7.0	4.45 ± 0.57

Table 4. Mean levels of clinical attributes in Diabetic nephropathy

	Blood urea	Serum creatinine	Triglycerides
Normal ranges	≤ 40 mg/dl 40-60 mg/dl Above 60 mg/dl	0.5 -1.5 % 1.5 above	Normal ≤ 150 mg/dl borderline 150-199 mg/dl high 200-499 mg/dl
Diabetic nephropathy patients	112.97 ±68.19	3.97 ± 1.30	257.9 ± 66.1
Control group	22.48 ± 14.49	0.92 ± 0.22	153.9 ± 8.5

Table 5. Percentages in clinical parameters involve in diabetic nephropathy and control group

Blood urea			Serum creatinine			Triglycerides		
Ranges	DN	control	Ranges	DN	control	Ranges	DN	control
≤ 40 mg/dl	0%	100%	0.5 -1.5 %	0%	100%	Normal ≤ 150 mg/dl	0%	37.7%
40-60 mg/dl	6.25%	0%	1.5 above	100%	0%	borderline 150-199 mg/dl	27%	62.2%
Above 60 mg/dl	93.7%	0%				high 200-499 mg/dl	72.9%	0%

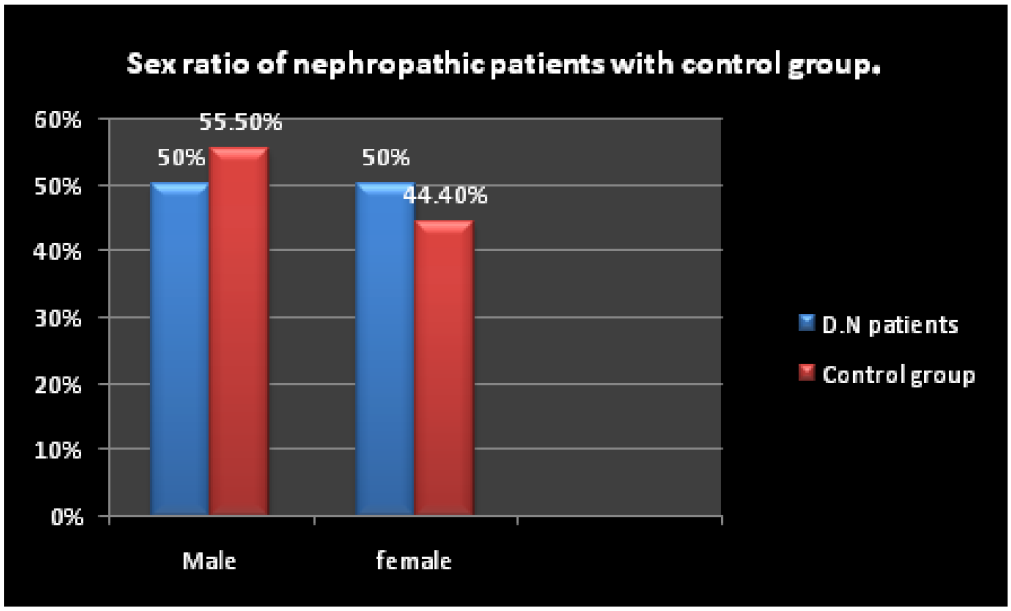

Figure 1. Sex ratio of diabetic nephropathy patients with control group

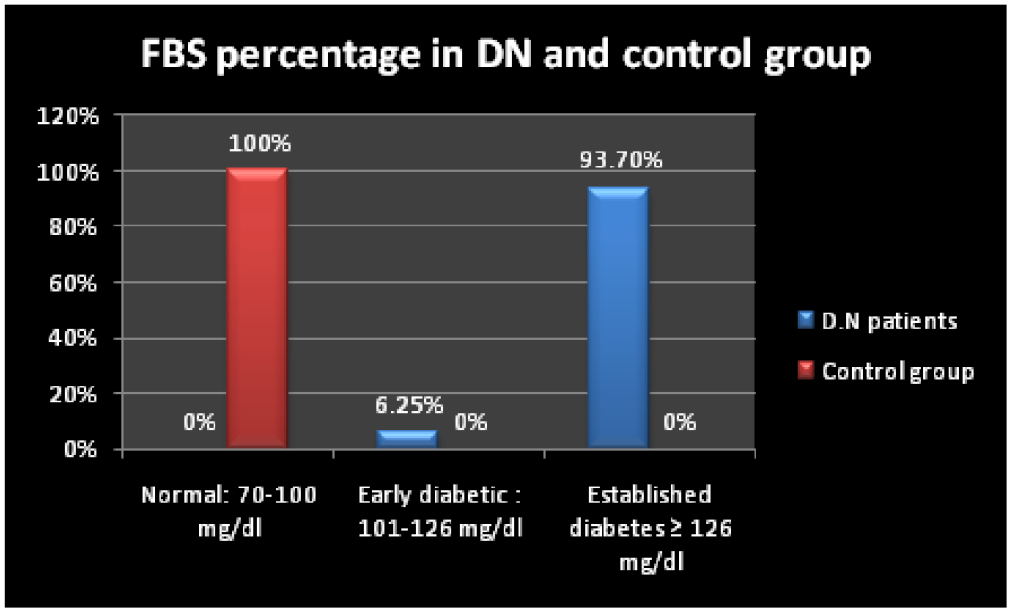

Figure 2. Fasting blood sugar in percentage in diabetic nephropathy with control group

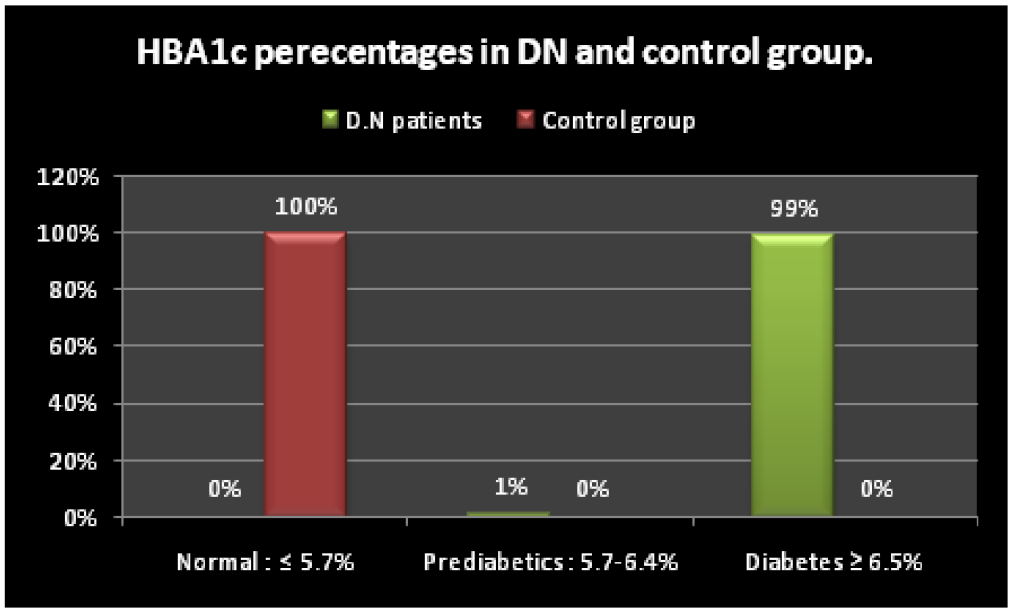

Figure 3. HBA1c percentages in diabetic nephropathy patients with control group

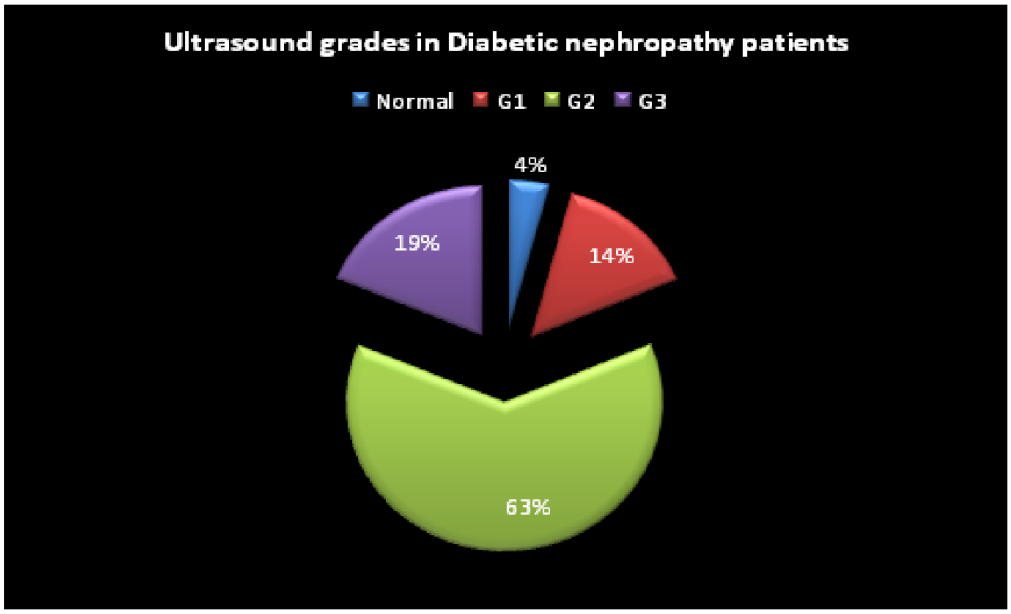

Figure 4. Ultrasonography grades in DN patients

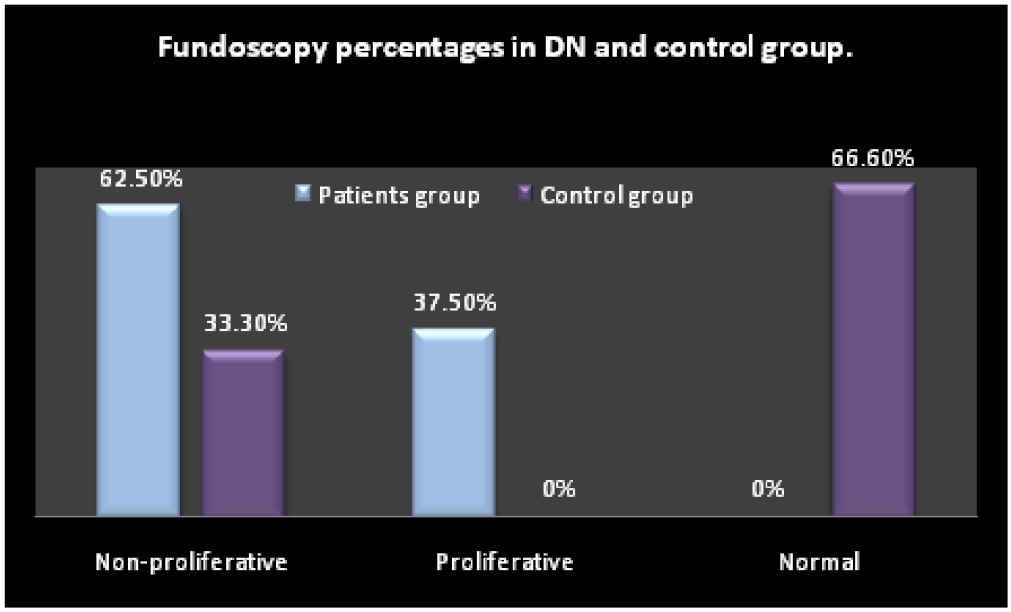

Figure 5. Fundoscopy in DN and control group