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ORIGINAL ARTICLE

# Incidence of Nephrotic Syndrome in Type 2 Diabetic Patients Presenting with Proteinuria

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***Authors' Contributions***

*1Conception & study design, Data collection & processing.*

*2Data analysis and/or interpretation, Drafting of manuscript.*

*3Data analysis and/or interpretation, Critical review.*

***Article info.***

*Received: May 05, 2021*

*Accepted: January 31, 2022*

***Funding Source:*** *Nil*

***Conflict of Interest:*** *Nil*

***Cite this article:*** *Masood A, Ujala S, Ali SA. Incidence of Nephrotic Syndrome in Type 2 Diabetic Patients Presenting with Proteinuria. RADS J Pharm Pharm Sci. 2021; 9(4):208-213.*

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## ABSTRACT

**Background:** Proteinuria in diabetic patients is usually interpreted as a clinical manifestation of diabetic nephropathy (DN). However, not all diabetic subjects with proteinuria have DN. Nondiabetic renal disease (NDRD) has been seen to cause proteinuria in diabetic patients. There is a wide variation of prevalence of NDRD. We conducted this study to determine the frequency of nephrotic syndrome in type 2 diabetic patients presenting with proteinuria.

**Methodology:** This study was a descriptive, cross-sectional study, conducted at department of Medicine, Bahawal Victoria Hospital, Bahawalpur. Total 92 individuals with type 2 diabetes between 30 and 60 years of age were enrolled in the study. Individuals with hypertension, chronic renal failure (CRF) and obstructive uropathy were excluded from the study. All individuals with nephrotic syndrome (presence/absence) were examined with appropriate medical history (diabetes duration, diabetes mellitus (DM) treatment, family history of kidney disease).

**Results:** The age group of this study was 30 to 60 years old, with an average age of 46.52 ± 7.23 years old. Most of the 53 patients (67.61%) were 51 to 60 years old. Among the 92 patients, 48 were male (52.17%) and 44 were female (47.83%). The average BMI was found to be 27.41 ± 2.74 kg / m². Nephrotic syndrome was found in 37 (40.22%) patients, while 55 (59.78%) had no nephrotic syndrome.

**Conclusion:** Our study concluded that the incidence rate of nephrotic syndrome is high in individuals with type 2 diabetes.

**Keywords:** Diabetes mellitus Type 2, proteinuria, nephrotic syndrome.

## INTRODUCTION

Diabetes (DM) is divided into 3 main types:

(i). Type I diabetes or insulin-dependent diabetes or adolescent diabetes,

(ii). Adult-onset type II diabetes or non-insulin-dependent diabetes

(iii). Gestational diabetes occurs during pregnancy with no previous h/o diabetes

The global incidence of diabetes is between 10% and 14%[1, 2]. Type 2 diabetes (formerly non-insulin-dependent diabetes mellitus (NIDDM) or adult diabetes) is a metabolic disorder characterized by high grade blood glucose levels, resistance to insulin and relative insulin deficiency[3]. Contrary to type 1 diabetes, which is due to pancreatic islets cells destruction leading to lack of insulin[4].

Diabetes is marked by varying points of high blood sugar, which is accompanied by biochemical changes in carbohydrate, protein, and lipid metabolism. In

essence, the adverse reactions of high blood sugar levels are of two types one is macrovascular and the second is microvascular[5]. It is reported that morphology and platelet function is impaired in people with diabetes and it is related to the pathological process and the high risk of vascular disease[6].

The frequency of diabetes (DM) is growing[7]. According to the USRDS report, the incidence of end-stage renal disease (ESRD) due to diabetes declined by 1.8% in 2008.when compared with the previous year. Despite this fact, In United States and many other countries/regions DM is still the most frequent cause of ESRD. About 20 to 40% of all DM patients eventually develop diabetic renal disease[8, 9]. Diabetic nephropathy (DN) is not the only renal disease amongst diabetic individuals. People with type 2 diabetes may have kidney disease other than diabetic nephropathy. These kidney diseases are called non-diabetic renal diseases (NDRD) and may be isolated or accompanied to DN[7].

Diabetic nephropathy (DN) is clinically manifested as proteinuria in diabetic individuals. But not all individuals with diabetes show proteinuria. Non-Diabetic renal disease (NDRD) has also been observed to cause proteinuria in diabetic patients[10]. The incidence of NDRD differed significantly[11, 12]. In one study, 64% of patients had non-diabetic renal failure and 36% of patients had diabetic glomerulosclerosis. The authors found that the occurrence of nephrotic syndrome in individuals with non-diabetic renal failure was 38.67% of the patients[13]. In another study, 67.7% of patients had nephrotic syndrome.

Since the occurrence of nephrotic syndrome in individuals with type 2 diabetes varies widely and no local data is available. This study was conducted to evaluate the incidence of nephrotic syndrome in individuals with type 2 diabetes. It will not only provide data on the degree of nephrotic syndrome in individuals with type 2 diabetes, but based on these results, we can provide some practical advice on how to consider non-diabetic renal disease in individuals with type 2 diabetes. Therefore, we encourage doctors to diagnose and treat non-diabetic nephropathy in individuals with type 2 diabetes to reduce its morbidity.

## METHODOLOGY

This study is a descriptive and cross-sectional study. It was conducted at Department of Medicine, Bahawal Victoria Hospital, Bahawalpur, Pakistan from May 23, 2018 to November 22, 2018. The hospital ethical committee approved the study. The calculated sample size for type 2 diabetes is 92, the confidence level is 95%, the error rate is 10%, and the percentage of nephrotic syndrome is 38.67%. Samples were selected according to following inclusion and exclusion criteria, All individuals with type 2 diabetes with proteinuria (as per current definition), diabetes duration>1 year, both genders, patients between 30 and 60 years old. The Exclusion criteria were**,** individuals with type 1 diabetes individuals with hypertension, individuals with chronic renal failure (medical history assessment and S / creatinine> 1.5 mg / dl), individuals with obstructive urinary tract disease (assessed on history, patients who do not want to participate in the study.

After CPSP approval, 92 patients were selected from Bahawal Victoria Hospital, Bahawalpur who met the inclusion criteria. Written consent was obtained from each patient. After an appropriate medical history (diabetes duration, diabetes treatment, family h/o kidney disease), all patients were examined for the nephrotic syndrome (presence/absence) according to the current definition. The researchers recorded all data in a pre-defined format.

We used SPSS version 20.0 for statistical analysis. The mean and standard deviation of age, type 2 DM duration, weight, height, and BMI were calculated. The frequency and percentage are calculated based on gender, place of residence (in rural/urban), DM treatment (yes/no), family h/o kidney disease (yes / no) and nephrotic syndrome (presence/absence).

Anatomically control modifiers such as age, gender, DM duration, BMI, place of residence (in villages/towns), DM treatment (yes/no) and family h/o kidney disease (yes / no). After stratification, chi-square was used to observe its effect on the frequency of nephrotic syndrome, and p-value ≤0.05 was considered as significant.

## RESULTS

The age range of this study was 30 to 60 years, with an average age of 46.52 ± 7.23 years. As shown in Table **1**, most of these 53 patients (67.61%) were between 51 and 60 years old.

Of the 92 patients, 48 were male (52.17%), and 44 were female (47.83%), with a male to female ratio of 1.1: 1. The average disease duration was 6.62 ± 3.85 years. The average height was found to be 167.33 ± 14.21 cm with an average weight of 76.89 ± 8.72 kg. The average BMI was 27.41 ± 2.74 kg / m² (Table **1**). Figure **1** shows the distribution of patients by place of residence. Table **2** shows the distribution of individuals with other disease variables.

The nephrotic syndrome was found in 37 (40.22%) patients, while 55 (59.78%) had no nephrotic syndrome.

When stratifying nephrotic syndrome by age group, no significant difference was found between different age groups, as shown in Table **3**. There was also no obvious difference between men and women differently. Table **3** also shows nephrotic syndrome according to disease duration and stratification of nephrotic syndrome with respect to BMI, taking treatment of DM, family h/o kidney disease and by living place. No significant difference was noted among the different stratification variables.

**Table 1. Distribution of patients according to age, duration of DM and BMI (n=92).**

| Age (in years) | No. of Patients | Male | Female | % |
|---|---|---|---|---|
| **30-45** | 39 | 22 | 20 | 42.39 |
| **46-60** | 53 | 26 | 24 | 57.61 |
| **Total** | 92 | 48 | 44 | 100.0 |
| **Duration (in years)** | **No. of Patients** | | **%** | |
| **≤5** | 55 | | 59.78 | |
| **>5** | 37 | | 40.22 | |
| **Total** | 92 | | 100.0 | |
| **BMI (in kg/m²)** | **No. of Patients** | | **%** | |
| **≤27** | 53 | | 57.61 | |
| **>27** | 39 | | 42.39 | |
| **Total** | 92 | | 100.0 | |

Mean ± SD = 46.52 ± 7.23 years (age)
Mean ± SD = 6.62 ± 3.85 years (duration of DM)
Mean ± SD = 27.41 ± 2.74 kg/m²

**Table 2. Distribution of patients with other confounding variables (n=92)**

| Confounding variables | | Frequency | % |
|---|---|---|---|
| **Taking treatment for DM** | Yes | 58 | 63.04 |
| | No | 34 | 36.96 |
| **Family h/o renal disease** | Yes | 51 | 55.43 |
| | No | 41 | 44.57 |

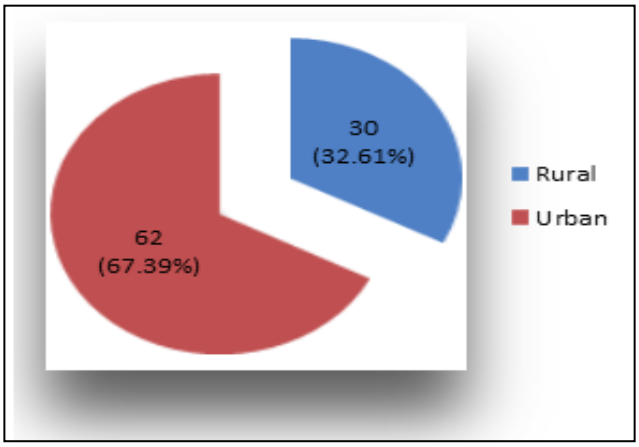


**Figure 1.** Distribution of patients according to place of living (n=92)

**Table 3. Stratification of nephrotic syndrome with respect to age, gender, BMI, place of living, duration of DM, taking treatment for DM and family h/o DM.**

| Age (years) | Nephrotic syndrome | | p-value |
|---|---|---|---|
| | Present | Absent | |
| 30-45 | 17 | 22 | 0.571 |
| 46-60 | 20 | 33 | |
| **Gender** | **Nephrotic syndrome** | | **p-value** |
| | Present | Present | |
| Male | 20 | 28 | 0.767 |
| Female | 17 | 27 | |
| **BMI (kg/m$^2$)** | **Nephrotic syndrome** | | **p-value** |
| | Present | Present | |
| ≤27 | 25 | 28 | 0.113 |
| >27 | 12 | 27 | |
| **Place of living** | **Nephrotic syndrome** | | **p-value** |
| | Present | Present | |
| Rural | 10 | 20 | 0.349 |
| Urban | 27 | 35 | |
| **Duration (years)** | **Nephrotic syndrome** | | **p-value** |
| | Present | Absent | |
| ≤5 | 23 | 32 | 0.703 |
| >5 | 14 | 23 | |
| **Taking treatment for DM** | **Nephrotic syndrome** | | **p-value** |
| | Present | Absent | |
| Yes | 23 | 35 | 0.886 |
| No | 14 | 20 | |
| **Family h/o DM** | **Nephrotic syndrome** | | **p-value** |
| | Present | Absent | |
| Yes | 23 | 28 | 0.287 |
| No | 14 | 27 | |

## DISCUSSION

The present study was conducted to determine the incidence of nephrotic syndrome in individuals with type 2 diabetes and proteinuria. The age range of the study participants was found to be 30 to 60 years, with an average age of 46.52 ± 7.23 years. Most of the 53 patients (67.61%) were 51 to 60 years old. Among the 92 patients, 48 were male (52.17%), and 44 were female (47.83%). The ratio of men to women was found to be 1.1: 1. Of the total 92 participants, 37 patients (40.22%) had nephrotic syndrome and 55 patients (59.78) %) did not develop nephrotic syndrome. In one study, 64% of patients had non-diabetic kidney disease and 36% of patients had diabetic glomerulosclerosis. The authors found that the incidence of nephrotic syndrome in individuals with non-diabetic renal failure was 38.67% of the patients [13]. In another study, 67.7% of patients had nephrotic syndrome.

Diabetes-induced nephropathy is one of the main causes of end-stage renal disease requiring renal replacement therapy. It is the leading cause of end-stage renal disease requiring renal replacement therapy in Japan and Western countries. In advanced type 2 diabetes, the occurrence of diabetic nephropathy is very high [14]. Individuals with type 2 diabetes are very likely to suffer from kidney disorders not linked to diabetes at any stage[15]. Iglesias et al. [16] stated that 44% of adults with urologic diseases had diabetes and proteinuria concentrations greater than 0.9 g / day had nephrotic range proteinuria. The right incidence of nephrotic syndrome in patients with macroalbuminuric diabetic nephropathy and in

nephrotic syndrome with Type 2 diabetes mellitus remains unclear.

It is harder to assess the occurrence of diabetic kidney disease of type 2 because it is hard to determine the onset of type 2 without diabetes[17]. Diabetic nephropathy is another unrelated condition which is not specifically caused by hematuria (MCNS). And renal disorders (MN)[18, 19], Glomerular kidney disorders are believed to cause renal failure[20]. Thus, the outcomes of MCNS and MN in middle-aged adults and in elderly patients can affect the effectiveness of drug therapy for type 2 diabetes.

It is now known that the clinical nephropathy (proteinuria) of individuals with type 2 diabetes may be situated histologically connected to the development of diabetic glomerulopathy or non-diabetic nephropathy or both. According to reports, 12–80% of individuals with type 2 diabetes and kidney disease suffer from non-diabetic renal failure[7, 21]. The large differences reported in these studies may be due to selection bias, because kidney biopsies are performed in clinically atypical patients. Diabetic nephropathy. In kidney biopsy studies, the incidence of NDRD in individuals with type 2 DM in Europe was 22%, and in Asians, 26.7%. Of the 52 individuals with clinical proteinuria[22], non-diabetic renal failure was accounting for 20 (38.5%), 32 had diabetic nephropathy (61.5%)[7], we reported that NDRD occurred in 43.7% of cases while results of biopsy showed DN in 56.3% of type 2 diabetes patients2157 A retrospective analysis of kidney biopsies in type 2 diabetes patients (n = 233) revealed 124 cases (53.2%) of NDRD. Pure diabetic glomerulosclerosis (DGS) 64 (27.5%), and 45 (19.3%) patients had both NDRD and DGS. This means that the exact incidence of non-diabetic nephropathy (NDN) in individuals with type 2 diabetes is unclear. The reported NDN for individuals with proteinuria2158–160 are 25% to 45% DM. Biopsy studies have shown that 25% to 50% of individuals with type 2 diabetes have unrelated glomerular lesions or are dependent on diabetic nephropathy[23, 24].

In one study, of 122 diabetic patients, 19 (8%) had both diabetic nephropathy and non-diabetic nephropathy. These patients have both clinical and pathological features (88.8%) of diabetic nephropathy with diabetic retinopathy. Diabetes has a long duration and increased membrane thickness. However, similarly, they also presented clinical results that are in conflict with diabetic nephropathy, such as hematuria, rapidly progressive renal failure, and significant proteinuria. 5 out of 10 patients (50%) developed immunoglobulin A (IgA) nephropathy, tubulointerstitial changes and Two patients (20%), two patients (20%) with proliferative glomerulonephritis (MPGN) and one patient (10%) with membranous nephropathy (MN)[25].

## CONCLUSION

Our results concluded that the incidence of nephrotic syndrome in type 2 diabetes individuals with proteinuria is very high. Therefore, we recommend that individuals with type 2 diabetes should be properly screened and must be treated as non-diabetic kidney disease to reduce their incidence.

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