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Original Research Article

# Clinical Study on Evaluation of Protein Tolerance Test as Marker for Early Renal Dysfunction in Type 2 Diabetes Mellitus

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**Abstract**

**Background:** A protein tolerance test can be highly helpful in selecting individuals who are most likely to benefit from an aggressive intervention by detecting incipient renal failure in those with normal GFR and serum creatinine values. This is crucial when assessing high-risk individuals including diabetics, people who have just undergone a kidney transplant, and people with polycystic kidney disease. PTT can be used to accurately predict the prognosis of a progressing renal disease and to evaluate the borderline renal donor. To demonstrate the value of the tubular stress test, standardisation and additional research are still needed. The purpose of this study was to examine the evolution of renal dysfunction with age and the duration of Type 2 Diabetes mellitus, as well as to assess the protein tolerance test as a marker for early renal impairment in Type 2 Diabetes mellitus.

**Method:** From March 2022 to February 2023, participants in this clinical trial were outpatients at the DMCH in Laheriasarai, Bihar. 208 instances altogether were split into two groups. In this study period, 108 cases in the study group and the remaining 100 cases in the control group were included. The study included people with Type 2 diabetes mellitus. For comparative purposes, 100 healthy, age- and sex-matched controls free of diabetes or its consequences were also included in the study.

**Results:** The prevalence of renal failure was found to be higher in individuals older than 60 years, at 179 (86.05%), compared to 33 (15.86%) in the group of patients who were 51–60 years old and 17 (8.17%) in the 41–50-year group. In contrast, in patients with renal dysfunction, 35 (16.8%) were found to have renal risk, and 43 (20.7%) had renal failure. It was discovered that normal working kidney would be able to lower urine protein after protein tolerance. In contrast to cases of renal failure, where eGFR decreased following protein tolerance, it was shown that kidneys with normal function responded to protein tolerance by increasing eGFR. In contrast to cases of renal failure, blood creatinine levels increased after protein tolerance good working kidney increased GFR. Renal failure risk is increased by Type II diabetes mellitus for an extended period of time.

**Conclusion:** Compared to patients with normal renal function or mild renal dysfunction, patients with renal failure exhibited more persistently elevated blood creatinine and sustained decreases in GFR.

**Keywords:** Impaired PTT, Marker, Renal dysfunction, Type 2 DM.



## Introduction

India is often referred to as the world's diabetic capital. Our nation has a high prevalence of diabetes mellitus, and its incidence is rising dramatically. Between 1985 and 2000, there were an estimated 177 million cases of diabetes worldwide[1], a sharp increase from the estimated 30 million cases in 1985. By 2030, more than 360 million people will develop diabetes worldwide, according to current trends. Both type 1 and type 2 diabetes are becoming more common worldwide, but type 2 diabetes is spreading much more quickly due to rising obesity and declining levels of physical exercise as nations become more industrialised. According to projections made for the entire world, people with diabetes will most likely be between the ages of 45 and 64 in 2030. The International Diabetes Federation (IDF) published the Diabetes Atlas, which states that there were approximately 40 million people with diabetes in India in 2007, 60 million in 2009, and that number is expected to reach almost 120 million by 2025, when every fifth diabetic subject in the world will be an Indian. Although diabetes is a leading cause of death, numerous research suggest that the disease is likely underreported as a cause of death. According to a recent estimate, diabetes accounts for over 3 million fatalities annually (1.7-5.2% of deaths globally) and is the fifth biggest cause of mortality globally.

Nearly 44 percent of all new occurrences of kidney failure[2] are caused by diabetes, which is also its most prevalent cause. Kidney failure, a dangerous disorder where the kidneys fail to remove waste from the body, affects more than 100,000 people. The last stage of chronic kidney disease (CKD) is renal failure. Diabetes can cause renal failure and CKD even when it is under control. Most diabetics do not have CKD that is advanced enough to result in renal failure. There are multiple interrelated risk factors for kidney disease and diabetes, including genes, food, and other illnesses including high blood pressure.[3] It has been discovered that having diabetes increases the likelihood of developing kidney failure, as do having high blood pressure and blood glucose levels. In order to start treatment and stop the progression of kidney impairment, it is necessary to detect subnormal renal function[4] at an earlier stage. The patient at risk of developing diabetes mellitus has been identified using the glucose tolerance test (GTT). The patient who has mild pancreatic dysfunction becomes disorganised by the stress of the glucose load in the GTT. It has been proposed that a protein tolerance test (PTT), similar to the GTT, may be useful in identifying people with subnormal renal function before they exhibit clinical symptoms. Although an elevated serum creatinine level is frequently thought to be the first indication of a kidney issue, this may no longer be the case. In order to identify endothelial dysfunction, microalbuminuria, another test to identify early renal failure, is currently employed. This emphasises the requirement for the renal tolerance test in patients with low glomerular filtration rate because by the time the blood creatinine levels rise, significant irreversible kidney damage has already occurred. A temporary hyperfiltration brought on by an acute oral protein load may indicate glomerular permselectivity loss. Acute protein load testing is therefore extremely helpful in identifying a silent glomerular filtration issue. We will be able to identify people with reduced functional reserve thanks to PTT's

stress. This idea is used in the current study to pinpoint the diabetic patients who are most likely to experience renal failure.

## Material and Methods

From March 2022 to February 2023, participants in this clinical trial were outpatients at the DMCH, Laheriasarai, Bihar. 208 instances altogether were split into two groups. In this study period, 108 cases in the study group and the remaining 100 cases in the control group were included. The study included people with Type 2 diabetes mellitus. For comparative purposes, 100 healthy, age- and sex-matched controls free of diabetes or its consequences were also included in the study. All patients with proteinuria, systemic hypertension, and renal failure due to Type 2 Diabetes mellitus were excluded from this investigation.

Clinical information and standard blood tests, such as postprandial and fasting blood sugar readings, were used to make the diagnosis of Type 2 diabetes mellitus. Clinical information, routine blood tests, measurements of baseline creatinine clearance and baseline creatinine clearance after a protein meal (100 g of protein as cottage cheese), and spot urinary protein estimation at baseline and after a protein meal were used to determine whether renal dysfunction existed or not. All the chosen patients received a high-protein meal after being diagnosed with Type 2 diabetes mellitus. Blood samples were taken after 8 hours of fasting for fasting blood sugar and after 2 hours of postprandial condition in order to determine renal dysfunction in type 2 diabetes mellitus. After a high-protein breakfast, blood samples were taken at 0, 30, 60, and 120 minutes to measure serum creatinine. Separated serum was kept in the refrigerator. From this serum, serum creatinine was determined. eGFR was calculated by using Cockcroft-Gault equation Estimated creatinine clearance (mL/min) = (140-age × body weight in kg)/72 × Plasma creatinine (mg/dL) Urine samples were collected at 0, and 120 minutes for Urine PCR .

With SPPS version 21.0, data analysis was carried out. This software was used to compute the range, frequencies, percentages, means, standard deviations, chi square, and "p" values. To determine the significance of a difference between two quantitative variables, the Kruskal Wallis chi-square test was performed. A significant association is considered to exist when the "p" value is less than 0.05.

## Results

The chosen cases Following the protein tolerance test, the renal functioning parameters of 108 in the study group and 100 in the control group were examined.

**Table 1: Age-related decline in renal function**

| | <40 years | 41-50 years | 51-60 years | >60 years |
|---|---|---|---|---|
| **Normal** | 208(100%) | 190(91.83%) | 175(84.14%) | 0% |
| **Injury** | 0% | 9(4.33%) | 18(8.65%) | 29(13.94%) |
| **Failure** | % | 9(4.33%) | 15(7.21%) | 179(86.05%) |

The analysis of the relationship between age and renal function is shown in Table 1. A higher rate of renal failure was observed in patients beyond the age of 60 (86.05%), compared to individuals between the ages of 51 and 60 (15.86%) and 41 to 50 (8.17%).

**Table 2: Urine protein-creatinine ratio with renal function**

| | PCR 0 minute | PCR 120 minutes |
|---|---|---|
| **Normal** | 208(100%) | 130(62.5%) |
| **Injury** | 0% | 35(16.8%) |
| **Failure** | 0% | 43(20.7%) |

In patients with renal dysfunction, 16.8% were found to have renal danger, and 20.7% had renal failure, whereas normal working kidneys would be able to lower urine protein after protein tolerance.(Table 2)

**Table 3: eGFR and Protein tolerance**

| | e-GFR pre meal (ml/min./1.73m$^2$) | e-GFR post meal (ml/min./1.73m$^2$) |
|---|---|---|
| **Normal** | 72.9 | 89.0 |
| **Injury** | 69.9 | 76.6 |
| **Failure** | 71.0% | 67.0 |

In contrast to cases of renal failure, when eGFR decreased after protein tolerance, Table 3 showed that kidneys with normal function responded to protein tolerance by increasing eGFR. (Table 3)

**Table 4: Serum creatinine and Protein tolerance**

| | S. creatinine pre meal (mg/dl) | S. creatinine post meal (mg/dl) |
|---|---|---|
| **Normal** | 0.90 | 0.76 |
| **Injury** | 0.86 | 0.90 |
| **Failure** | 0.93 | 0.99 |

Table 4 demonstrates that, in contrast to cases of renal failure, normal working kidney increased GFR following protein tolerance.

**Table 5: Duration of diseases with Renal function**

| | <6 years | 6-8 years | >8 years |
|---|---|---|---|
| **Normal** | 97% | 47% | 0% |
| **Injury** | 3% | 48% | 16% |
| **Failure** | 0% | 8% | 84% |

Table 5 demonstrates how having Type II Diabetes for a long time increases the chance of renal failure.

## Discussion

Analysis of renal function was done on the two groups. 97% of patients in the control group had normal renal function, as opposed to 61% in the test group. In the test group, 16.8% of patients had renal damage, compared to 3% in the control group. Compared to 20.7% of patients in the test group, no patients in the control group experienced renal failure. The GFR decreased with age, as was the case in the majority of studies[5]. In this study, around 86.05% of patients over 60 developed renal failure, compared to only 24% of patients under 60. After protein tolerance, it was discovered that normal working kidneys could lower the amount of protein in the urine, however in patients with renal dysfunction, renal risk and renal failure were observed in 17% and 21% of patients, respectively. In this study, it was discovered that patients with renal injury and renal failure cases had post-protein challenge mean creatinine levels that remained consistently higher than those with normal renal function.

This suggests that it could be a valuable predictor of renal reserve. The drop in post-protein challenge eGFR-2 was also statistically significant, falling to 67 ml/kg/1.73 m2 in renal failure from 89 ml/kg/1.73 m2 in normal renal function. According to the study, renal failure was substantially correlated with an increase in diabetes duration [6].

This study by Gall M, et al. [6] found that both Type 2 and Type 1 diabetes were related with renal failure as patients' ages and diabetes duration increased [7]. Age was not a more significant risk factor for Type 2 diabetes than diabetes duration was [8-11]. Proteinuria and Type 1 and Type 2 diabetic retinopathy were both substantially linked to renal failure in the same study. In our study, 38% of patients with aberrant urine protein creatinine ratios showed renal impairment, which was also seen.[12,13]

## Conclusion

Compared to patients with normal renal function or mild renal dysfunction, patients with renal failure exhibited more persistently elevated blood creatinine and sustained decreases in GFR. Renal function also decreased as people aged. An independent risk factor for renal failure was discovered to be proteinuria. It was discovered that patients with long-term diabetes and poor glycemic control have a higher risk of developing early renal dysfunction and injury than those with short-term diabetes with effective glycemic management.

When a patient's GFR and serum creatinine are both normal, a protein tolerance test can be helpful in identifying early renal failure. It makes it possible to start an intensive early intervention. In high-risk patients with conditions such diabetes, hypertension, isolated kidney disease, polycystic kidney disease, and post-renal transplantation, a protein tolerance test may be helpful.

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