Correlation of Anemia and Serum Transferrin in Diabetic Nephropathy

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Abstract

Background: End Stage Renal Disease is the common cause of morbidity and mortality in patients suffering from diabetes and hypertension. Loss of transferrin and renal impairment in diabetic patients might lead to microcytic anaemia. Progression of nephropathy in these patients can be prevented by checking the hemoglobin levels. Objectives: This study is aimed at identifying the relationship of transferrin levels and anaemia in diabetic nephropathy. Methods: The study included 100 patients who were categorized as 20 normoalbuminuric, 40 microalbuminuric and 40 macroalbuminuric based on urine albumin levels. Serum Transferrin, Hemoglobin were measured in all the three groups. Results: The data obtained concludes that the levels of hemoglobin are significantly reduced in macroalbuminuric (9.0 ± 1.61) than microalbuminuric (11.5 ± 1.71) as compared to normoalbuminuric (13.1 ± 1.91) patients. Serum transferrin levels were significantly reduced in macroalbuminuria (207 ± 33.7) as compared to normoalbuminuria (263 ± 51.8), which in correlation to hemoglobin levels. Conclusion: Anaemia was often seen at an early stage in diabetic nephropathy than in patients with chronic kidney disease. It is, therefore, crucial to monitor anaemia to prevent the progression of renal disease in diabetic patients manifested as microalbuminuria. Plasma transferrin levels are decreased in macroalbuminuria though the synthesis is increased in diabetic nephropathy as the response doesn't compensate for the loss of transferrin in the urine. Further understanding of the mechanism and providing the therapy may improve patient outcomes.

Keywords: End Stage Renal Disease, Transferrin, Diabetic Nephropathy, Albuminuria.

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INTRODUCTION

Patients with diabetes suffer the implications of impaired renal function earlier in the course of their disease than do their non-diabetic counterparts [1-3]. In diabetic nephropathy, anaemia tends to be more severe than in non-diabetic renal disease and occur at an earlier stage of the illness [4]. However, because most patients with early diabetic nephropathy have little overt renal impairment, primary care physicians are often the first-line health care providers and may not be aware of the critical importance of screening for anaemia. Thus anaemia could typically be recognised or untreated [5].

Anaemia outlined as haemoglobin <13 gm/dl in males and <12 gm/dl in females [6, 7]. Diabetes is the single commonest reason behind end-stage renal disease and thus, the foremost common reason behind nephritic anaemia [8]. The predominance of harm to the renal interstitium, systemic inflammation and autonomous nephropathy have all been suggested as contributing to anaemia in diabetic nephropathy [9]. Microalbuminuria develops after five years of diabetes whereas positive dipstick proteinuria develops 5 to 10 years after the onset of microalbuminuria and is associated with progressive loss of renal function [10]. Validating clues for nephropathy include enlarged kidneys and evidence of diabetic retinopathy. Anaemia is a common accompaniment of diabetes, particularly in patients with albuminuria or decreased renal function. Studies in patients with renal impairment suggest that deleterious effect begins with haemoglobin <11 gm/dl meaning that 7% of patients with diabetes may benefit from intervention according to current guidelines [11]. Studies have shown the importance of iron stores in the development and progression of anaemia in patients with diabetes.

Transferrin is the principal plasma protein for the transport of iron; each molecule of transferrin has affinities for iron stores in the urine. Further understanding of the mechanism and providing the therapy may improve patient outcomes.
acute-phase protein with a molecular weight of eighty kilo daltons synthesised with in the liver [12]. Plasma levels of transferrin are regulated primarily by the availability of iron [13]. Tranferrinuria, particularly with impaired renal functions and proteinuria, also contribute to iron deficiency anaemia [14]. Very few studies have been done on transferrin levels in diabetes with and without nephropathy. The present study aims to elicit the relationship of transferrin levels and anaemia in diabetic nephropathy.

MATERIALS AND METHODS

The current study is a Cross-Sectional study conducted in our hospital from July 2018 to June 2019. The study had 100 patients who were categorised as the group I, 20 diabetics with normoalbuminuria (<30 mg/day), group II, 40 diabetics with microalbuminuria (30-300 mg/day) and group III, 40 diabetics with macroalbuminuria (>300 mg/day).

Inclusion Criteria Include: Patients with type 2 diabetes of age >35 years.

Exclusion Criteria Includes: Acute infections, Congestive Cardiac failure, Uncontrolled hypertension, other causes of iron deficiency anaemia and pregnancy.

The study was approved from the ethics committee of our Institute. Patients were provided with complete information, and written consent is obtained.

Diagnosis of diabetes is based on WHO criteria, i.e.; FBG > 126 mg/dl or postprandial glucose > 150 mg/dl, similarly anemia being defined as hemoglobin <13gm/dl in males and <12gm/dl in females.

Biochemical Methods

- **Glucose** – GOD POD method
- **Hemoglobin** – Hematology Analyser
- **HbA1c** – Turbidometric method
- **Creatinine** – Enzymatic method
- **Urine microalbumin** – Turbidometric method

Estimation of Serum Transferrin

Serum Transferrin was determined by Immunoturbidometric method. Mixing of the sample with a precise antigen to a solution having corresponding anti-serum in a well-defined ratio, it is possible to have turbidity. Plotting on the calibration curve absorbance values and concentration for every single sample may determine the level of each sample.

|                | Blank | Standard | Test  |
|----------------|-------|----------|-------|
| Reagent        | 500 µL| 500 µL   | 500 µL|
| Sample         | -     | 6 µL     | -     |
| Calibrator     | -     | -        | 6 µL  |

Mix carefully and incubate at 37°C for 5 minutes and measure the absorbance of test and calibrator against blank and calculate the test.

STATISTICAL METHODS

All the values were calculated as the mean ± standard deviation. P-value was calculated, and <0.05 is taken as significant. Student T-test is used. Licensed SPSS software is used for the analysis of the data.

RESULTS

Table-1 shows the correlation between normoalbuminuria (<30mg/day) and microalbuminuria (30-300mg/day) in type 2 diabetes. Urine albumin is significantly (p=0.0003) elevated in microalbuminuria as compared to normoalbuminuria. Haemoglobin levels were not decreased significantly in microalbuminuria patients as compared to normoalbuminuria. Even serum transferrin and serum creatinine as haemoglobin have no significant change. A significant elevation of HbA1c, an index of blood glucose in the past three months is observed in microalbuminuria when compared to normoalbuminuria.

|                | Group I (< 30 mg/day) | Group II (30-300 mg/day) | p-Value |
|----------------|------------------------|--------------------------|---------|
| Urine Albumin (mg/day) | 21 ± 8.9               | 144.2 ± 88.0             | 0.0003  |
| Serum Transferrin (mg/dl) | 263 ± 51.8            | 302 ± 63.8               | 0.1520  |
| Hemoglobin (gm/dl)      | 13.1 ± 1.91            | 11.5 ± 1.71              | 0.064   |
| HbA1c (%)               | 6.09 ± 0.5             | 7.5 ± 0.7                | 0.0001  |
| Serum Creatinine (mg/dl) | 0.93 ± 0.3            | 1.0 ± 0.27               | 0.241   |

|                | Group II (30-300 mg/day) | Group III (>300 mg/day) | p-Value |
|----------------|--------------------------|-------------------------|---------|
| Urine Albumin (mg/day) | 144.2 ± 88.0            | 778.3 ± 339.9           | 0.0001  |
| Serum Transferrin (mg/dl) | 302 ± 63.8              | 207 ± 33.7              | 0.0006  |
| Hemoglobin (gm/dl)      | 11.5 ± 1.71             | 9.0 ± 1.61              | 0.004   |
| HbA1c (%)               | 7.5 ± 0.7               | 9.6 ± 1.7               | 0.002   |
| Serum Creatinine (mg/dl) | 1.0 ± 0.27              | 1.5 ± 0.24              | 0.002   |
A significant decrease of Hb is observed in macroalbuminuria as compared to microalbuminuria. A little elevation of serum Creatinine is observed.

Table III compares the normoalbuminuria with microalbuminuria in type 2 diabetes. All the parameters show a significant variations in normoalbuminuria compared to macroalbuminuria with type 2 diabetes.

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