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Original Research Article

Study of correlation between adequacy of dialysis and glycemic control in patients of type 2 diabetes mellitus with chronic kidney disease stage 5

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ABSTRACT

Background: The adequacy of haemodialysis in patients of type 2 diabetes mellitus with chronic kidney disease stage 5 depends on several clinical as well as laboratory parameters. Previous studies from Western literature have identified several clinical and laboratory markers for predicting adequacy of dialysis. There is a dearth of literature regarding the same in Indian patient populace. Authors aimed to find correlation, if any, between glycemic control and adequacy of dialysis in this cohort of patients.
Methods: A set of 200 patients of type 2 diabetes mellitus who have undergone hemodialysis at a tertiary care hospital were included in the study. Random blood sugar (RBS), Glycated hemoglobin (HbA1c) were measured at admission. After 4 hours of dialysis, the urea reduction ratio (URR) and Kt/V was measured for each patient. The correlation coefficient as well as linear equation of the association between these variables were calculated. Standard statistical method and software were used in the process.
Results: The study revealed a linear negative correlation between the variables RBS, HbA1c and URR as well as Kt/V. This suggests the importance of pre dialysis glycemic control in patients undergoing hemodialysis.
Conclusions: Authors formulate the hypothesis that glycated hemoglobin and random blood sugar at admission correlate well with the outcome and adequacy of dialysis in patients of stage 5 chronic kidney disease undergoing haemodialysis. Good glycemic control (HbA1c <6.5 % and RBS <120 mg/dL) have shown to be important predictive markers of adequate dialysis. The hypothesis needs to be tested with a larger study.

Keywords: Adequacy, Chronic kidney disease, Glycated hemoglobin, Haemodialysis, Kt/V, Random blood sugar, Urea reduction ratio

INTRODUCTION

Diabetes mellitus is the leading cause of end-stage renal disease (ESRD) globally. Adequacy of dialysis is a vital but often clinically ignored parameter. Several studies have underlined the importance of monitoring of adequacy of dialysis. In a landmark study from Iran, the adequacy of dialysis indices among Iranian patients was below the standard levels and it was necessary to consider measures to improve dialysis efficacy.[1] Literature is lacking regarding the same in Indian patients. The optimal utilisation of dialysis services in patients of type 2 diabetes mellitus is undergoing a paradigm shift. There is uncertainty surrounding the optimal glycemic target, although recent epidemiologic data suggest that HbA1c ranges of 6% to 8%, as well as 7 to 9%, are associated with increased survival rates among diabetic dialysis patients.[2]

The parameters for assessment of dialysis adequacy have been extensively reviewed; the Urea Reduction Ratio (URR) and Kt/V are the commonest parameters employed for this purpose. Liang et al, noted that targeting a URR ≥0.67 provides a simplified means of assessing adequacy of hemodialysis in patients with kidney disease. Use of URR enhanced ability to assess delivery of small solute clearance and improve adherence with clinical practice guidelines in kidney injury.[3]

Another useful parameter for dialysis adequacy is Kt/V where, K - dialyzer clearance of urea, t - dialysis time, V - volume of distribution of urea, approximately equal to patient's total body water.[4,5] The parameter has been recommended by National Institute of Diabetic and Digestive and Kidney Diseases.[6] However, there has been questions raised regarding the utility of conventional parameters for adequacy of dialysis: Biniaz et al concluded that Kt/V is not the best criterion and one cannot be assured of dialysis adequacy solely based on this criterion.[7]

In a large series by Rezaiee, hemodialysis adequacy in 56.4% of patients was optimal, in 29.7% near optimum, and in 13.9% less than optimal. Statistical tests showed a significant correlation between hemodialysis adequacy and age (p = 0.05), prehemodialysis systolic blood pressure (BP) (p = 0.02) and diastolic BP (p = 0.04), the duration of hemodialysis in months (p = 0.02), and patients' sex (p = 0.01). There was no significant correlation between hemodialysis adequacy and the number of hemodialysis sessions per week (p = 0.20), interdialytic weight gain (p = 0.40), prehemodialysis blood urea nitrogen (p = 0.40), creatinine (p = 0.10), hemoglobin (p = 0.20), hematocrit (p = 0.08), venous access type (p = 0.30), needle distance and direction (p = 0.70), underlying causes of end-stage renal disease (p = 0.50).[8]

Numerous studies have established a link between prior clinical/ laboratory findings and adequacy of dialysis. A study by Sheikh et al, showed positive correlation between dialysis dose and hemoglobin, serum albumin, normalized protein catabolic rate.[9]

Adas et al, noted that in a large group of dialysed patients, mean Kt/V and URR were 1.06±0.05 and 54.4±19.3, respectively. There was no significant difference between men and women (1.06±0.47 versus 1.04±0.55, p = 0.863) and (54.7±19.59 versus 53.81±19.17, p = 0.296). There was no significant association between hemodialysis adequacy and any of the variables such as sex, age, presence of chronic diseases or BMI.[10] In another series - Adas et al, conducted an observational cross-sectional study that was conducted in July 2012. Blood tests, weight and blood pressure were measured before and after hemodialysis. Single-pool Kt/V and urea reduction ratio (URR) were calculated. The targets based on the National Kidney Foundation Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines were Kt/V ≥1.2 and URR ≥65%. Of the 64 patients, 41 (64.1%) were males. The mean age of the patients was 58.13±17.2 years. The mean body mass index (BMI) was 25.04±5.01 kg/m^2. The mean Kt/V and URR were 1.06±0.05 and 54.4±19.3, respectively. There was no significant difference between men and women (1.06±0.47 versus 1.04±0.55, p = 0.863) and (54.7±19.59 versus 53.81±19.17, p = 0.296). Only 25 (39.1%) patients achieved the Kt/V goal and only 22 (34.4%) had target URR, and there was no significant association between hemodialysis adequacy and any of the variables such as sex, age, presence of chronic diseases or BMI. Serum potassium levels post-dialysis were significantly lower in patients who reached the target Kt/V (mean = 3.44±0.48 versus 3.88±0.48, p = 0.001). Most patients were inadequately dialyzed and a large percentage of the patients did not attain the targets. Attempts to achieve the desired goals are necessary. It is important to calculate Kt/V or URR and individualize the dialysis doses for each patient.[11]

In a study by Tascona et al, a high proportion of hemodialysis patients with diabetes had inadequate glycemic control, particularly those with longstanding disease.[12] van Diepen et al, have developed a prediction model containing seven predictors (age, smoking, history of macrovascular complications, duration of diabetes mellitus, Karnofsky scale, serum albumin and hemoglobin level) has been identified in order to predict 1-year mortality for diabetic incident dialysis patients.[13]

In the metanalysis Couchoud et al, available evidence derived from observational studies on chronic diseases and dialysis, were found to be inconsistent. Therefore evidence-based arguments indicating that HD or PD as first treatment may improve patient-centred outcomes in diabetics with ESKD are lacking.[14]

Heymati et al, concluded that no significant correlation was detectable between Kt/V and TAC with either body mass index and albumin or C-reactive protein. Based on the Kt/V values, patients with adequate dialysis had slower decrease in the PCR (p <0.001). Their results indicate that adequacy of dialysis is correlated with patients' nutritional status. No correlation was observed between dialysis adequacy and inflammatory status.[15]

Vaeleria et al, designed a study to explore the relationship between parameters of glycemic control of T2DM in RRT; the studied 23 patients on hemodialysis (HD), 22 on peritoneal dialysis (PD), and compared them with 24 T2DM patients with normal renal function (NRF). On four consecutive days, 10 assessments of capillary blood glucose [4 fasting, 2 pre- and 4 postprandial (post-G) and average glucose (AG)], random glycemia, and HbA1c in all patients. Pre-prandial blood glucose was greater in patients on RRT compared with NRF. Correlations between AG and HbA1c were 0.76 for HD, 0.66 for PD, and 0.82 for NRF. The regression lines between AG and

HbA1c were similar for patients on HD and with NFR, but they were displaced upward for PD. Similar HbA1c values in PD patients may correspond to greater levels of AG than in HD or NRF patients.[16]

Duong et al, noted that poor glycemic control appears associated incrementally with higher mortality in PD patients. Moderate to severe hyperglycemia is associated with higher death risk especially in certain subgroups.[17]

Author aimed to find correlation, if any, between prior glycemic control (measured by glycated hemoglobin and random blood sugar) and adequacy of dialysis.

METHODS

Patients undergoing regular hemodialysis in the period Jun 2018 to Dec 2019 (18 months), and total of 200 patients in this period were included in the study.

The study was carried out in a tertiary care referral hospital, serving patients from all over India.

Inclusion criteria

Patients who were known cases of type 2 diabetes mellitus for more than 10 years, who have developed stage 5 chronic kidney disease and undergoing regular hemodialysis in the dialysis center of a large tertiary care hospital between were selected. The patients were all within the age group 40 years - 70 years.

Exclusion criteria

Patients requiring hemodialysis for any purpose other than chronic kidney disease due to type 2 diabetes mellitus, and patients who underwent adequate dialysis in less than 4 hours duration were excluded from the study. Patients having a hemoglobin less than 8 g/dL were also excluded, due to falsely elevated results of HbA1c in such patients. Patients who had undergone blood transfusion in the last 3 months were excluded to rule out the possibility of an erroneous HbA1c measurement.18 Critically ill type 2 diabetic patients with chronic kidney disease admitted in ICU who required dialysis were also excluded from the study, to rule out acute phase glycemic changes.

Measurement of glycemic control

For all patients included in the study, Glycated hemoglobin (HbA1c) and random blood sugar (RBS) was measured at admission. Measurements were done only at the first instance of the patient presenting to the dialysis centre.

Measurement of dialysis adequacy

All patients underwent a single session of hemodialysis of 4 hours duration Fresenius 5008 hemodialysis machine. The adequacy of hemodialysis was checked with URR and Kt/V post dialysis.

HbA1c and random blood sugar (RBS) were measured on a Siemens Dimension XL fully automated analyser. Blood urea nitrogen (BUN) was measured pre-dialysis and post dialysis. URR was calculated as

$$URR = 100\% \times \frac{\text{(Predialysis BUN - Postdialysis BUN)}}{\text{Predialysis BUN}}$$

Kt/V was calculated from the dialysers clearance (K ml/min) as reported by the dialysis machine, time for dialysis (t = 4 hrs = 240 minutes) and the volume of distribution of urea (V), which was determined from patient's body weight (60% of body weight).

Correlation was calculated between the four parameters: HbA1c, RBS, URR and Kt/V.

Statistical analysis was carried out with Libreoffice Calc software.

RESULTS

The correlation coefficient (r) between HbA1c and Kt/V was found to be -0.83, suggesting a negative, linear correlation between the two variables; this suggests a better dialysis outcome with better glycemic control (Figure 1).

Because all the patients belonged to a carefully selected cohort and underwent similar investigations as well as dialysis procedure in the same setup, this result represents the role of glycemic control in predicting outcome of dialysis.

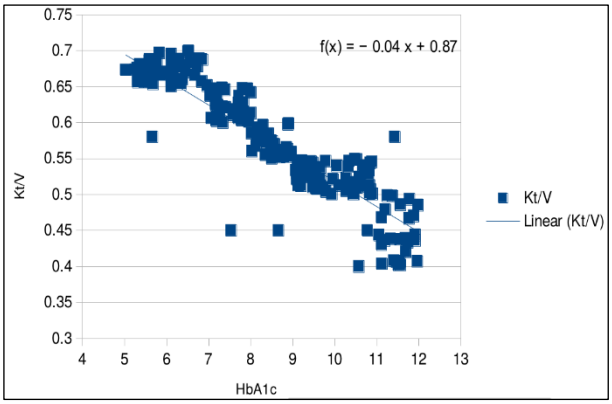

Figure 1: Correlation between glycated hemoglobin and Kt/V.

Similarly, URR was negatively correlated to HbA1c (r = -0.90) (Figure 2).

This shows a better correlation with HbA1c than Kt/V, suggesting the relative importance of URR over Kt/V in

the outcome of dialysis in patients of diabetic kidney disease.

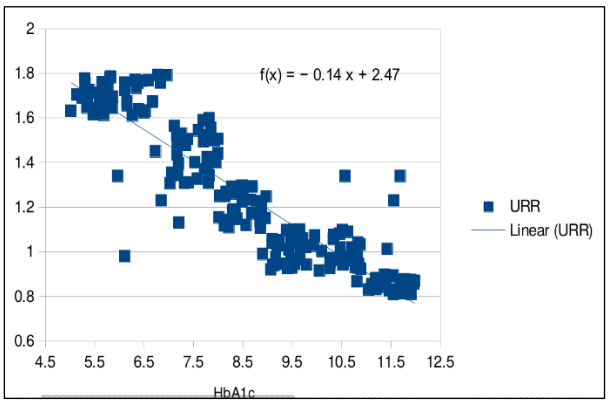

Figure 2: Correlation between glycated hemoglobin and URR.

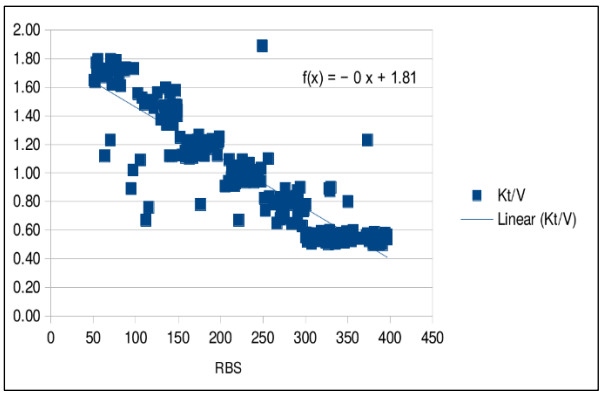

Figure 3: Correlation between random blood sugar and Kt/V.

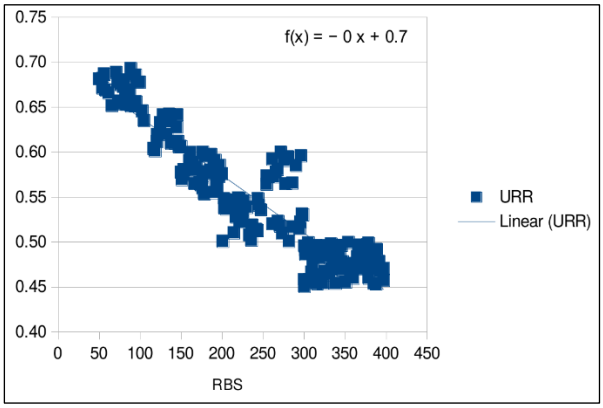

Figure 4: Correlation between random blood sugar and URR.

Random blood sugar was also inversely correlated with Kt/V (r = - 0.89) (Figure 3) and URR (r = -0.91) (Figure 4). Random blood sugar represents the instantaneous glycemic state of the patient just before the commencement of dialysis. This suggests both long term glycemic control (as indicated by HbA1c) and short-term glycemic control (measured by random sugar) have an impact of adequacy of dialysis. Based on our results, we recommend assessment of these two parameters in all patients of diabetic kidney disease before commencement of dialysis.

The results indicate that apart from demographic and clinical criteria, indicators specific to glycemic control play an important prognostic role in predicting the outcome of dialysis. Specifically, the good linear correlation between short term and long-term glycemic control and the dialysis adequacy parameters urea reduction ratio (URR) and Kt/V indicate that glycemic control is an independent prognostic marker fr dialysis adequacy, irrespective of clinical and demographic criteria.

Confounding factors like anemia, age (patients belonged to the age group 40 years to 70 years only) and acute infections (patients with sepsis/ acute infections admitted in ICU requiring dialysis were excluded) were ruled out in the study by carefully selecting the patient cohort. Only stable patients undergoing regular hemodialysis in this centre were included.

DISCUSSION

Hemodialysis is the modality of choice in renal replacement therapy in patients of chronic kidney disease stage 5 (End stage renal disease). However, there have been few studies in Indian population regarding the prognostic markers of adequacy of hemodialysis in diabetic patients. The present study attempts to correlate the pre-dialysis random sugar (RBS) and glycated hemoglobin (Hb A1c) and the two parameters urea reduction ratio (URR) and Kt/V as the indicators of adequacy of dialysis.

HbA1c as a marker of glycemic control is widely accepted; however, its efficacy in monitoring output of dialysis has been questioned. Some authors recommend glycated albumin as a better prognostic marker.[20] In the present study, we have followed KDOQI guidelines and accepted Kt/V and URR as indicators of dialysis adequacy.

Kt/V and URR are globally recognised indicators of adequacy of dialysis. On average, a Kt/V of 1.2 is roughly equivalent to a URR of about 63 percent. Thus, another standard of adequate dialysis is a minimum Kt/V of 1.2. The Kidney Disease Outcomes Quality Initiative (KDOQI) group has adopted the Kt/V of 1.2 as the standard for dialysis adequacy. Like the URR, the Kt/V may vary considerably from treatment to treatment because of measurement error and other factors. So, while a single low value is not always of concern, the average Kt/V should be at least 1.2. In some patients with large fluid losses during dialysis, the Kt/V can be greater than 1.2 with a URR slightly below 65 percent-in the range of 58 to 65 percent. In such cases, the KDOQI

guidelines consider the Kt/V to be the primary measure of adequacy.[6]

The present study has established a negative correlation between.

- pre-dialysis HbA1c and URR
- pre-dialysis HbA1c and Kt/V
- pre-dialysis RBS and URR
- pre-dialysis RBS and Kt/V

This study results indicate that prior glycemic control, both long term (HbA1c) and short term (RBS) have a direct bearing on the outcome of dialysis, specifically the two parameters URR and Kt/V. This is in conjunction with findings in earlier studies, such as that by Valeria et al.[16]

Strict glycemic control (HbA1c <6.5 % and RBS <120 mg/dL) was recommended before undertaking dialysis to improve outcomes of dialysis and ensure adequacy of dialysis in all patients of type 2 diabetes mellitus with CKD stage 5.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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