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Hemoglobin A1c levels in maintenance hemodialysis patients in India

Madhusudan Vijayan[1,2], Sanjay Moses[1], Sam Nishanth[1], Rajeevalochana Parthasarathy[1], Deepu George[1], Milly Mathew[1], Georgi Abraham[1,3,2*], Ashok Kumar Das[3], Viswanathan Mohan[4]

[1]Madras Medical Mission Hospital, Chennai, India
[2]Tamilnadu Kidney Research Foundation, Chennai, India
[3]Pondicherry Institute of Medical Science, Pondicherry, India
[4]Dr. Mohan's Diabetes Specialities Center, Chennai, India

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ABSTRACT

Introduction: The optimal hemoglobin A1c (glycated hemoglobin; HbA1c) target in diabetic patients on haemodialysis is not established. Most guidelines suggest a HbA1c target of 7%-8%%.
Objectives: There is paucity of Indian data on the optimal HbA1c values to be targeted in dialysis patients, and hence this prospective study was undertaken to address this gap.
Patients and Methods: This prospective study was conducted in 61 prevalent maintenance haemodialysis patients with type 2 diabetes mellitus. We looked at the association of HbA1c with 1-year survival and hemoglobin values.
Results: At the end of one year, 38 patients had survived, 10 patients died, 3 patients were transferred to continuous ambulatory peritoneal dialysis, and 10 patients were transferred to other centres. There was a significant relationship between HbA1c levels and blood hemoglobin values (r=0.245, $P=0.05$). The HbA1c values of non-survived patients (7.350 ± 1.834) were higher than those survived (6.768 ± 1.602), though not statistically significant ($P=0.326$).
Conclusion: This study shows that in diabetic nephropathy patients, poor glycemic control could be a factor for decreased survival rates on haemodialysis. However, larger prospective studies are required to establish the relationship.

Implication for health policy/practice/research/medical education:
We found an association between increased HbA1c and mortality in Indian diabetic patients undergoing hemodialysis, though not statistically significant. Higher HbA1c levels may lead to increased mortality in this population, which needs to be confirmed by larger prospective studies.
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Original

Introduction

Glycated hemoglobin (hemoglobin A1c; HbA1c) levels in uremic patients may overestimate glycemic status as they are influenced by a variety of factors including anemia, frequent blood transfusions, decreased lifespan of erythrocytes, and susceptibility of haemoglobin to glycosylation (1-3). While in the general population, several trials have demonstrated the long-term benefits of intensive glycemic control, the optimal HbA1c target in diabetic patients on haemodialysis is not established. Dialysis patients may be more prone to hypoglycemia due to various factors including malnutrition, decreased insulin clearance, and decreased renal gluconeogenesis (4-7). Thus, intensive glycemic control may be associated with increased mortality as shown by several studies (8-10). Most guidelines suggest a HbA1c target of 7%-8% (11,12).

Objectives

There is paucity of Indian data on the optimal HbA1c values to be targeted in dialysis patients, and hence this prospective study was undertaken to address this gap.

Patients and Methods

Study design

This prospective study was conducted in 61 prevalent maintenance hemodialysis (HD) patients with type 2 diabetes mellitus at the Madras Medical Mission

***Corresponding author**: Georgi Abraham, Email: abraham_georgi@yahoo.com

Hospital, Chennai and Pondicherry Institute of Medical Science, Pondicherry between July 2015 and June 2016. All patients currently undergoing dialysis who were known diabetics were included in this study. We collected the following clinical details and laboratory measurements: demographic details, dietary patterns, vintage of haemodialysis, dialysis prescription, urine output, haemoglobin A1c (using high performance liquid chromatography, D10, Bio-Rad), blood hemoglobin levels, blood pressure, treatment history and echocardiographic details. Five patients had previously received percutaneous coronary intervention (4 M/1 F) and three patients (3 M/0 F) had received coronary artery bypass graft. We followed up these patients after one year. The number of HD per week varied from 2 to 4 sessions. Each HD session lasted for 4 hours. We looked at the association of HbA1c with 1-year survival and hemoglobin values.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. This study was approved by ethics committee of Madras Medical Mission hospital. All participants were informed about the objectives of the study and assured that the information will remain confidential. Participants also signed out consent forms.

Statistical analysis

Statistical analysis was done using EZAnalyze software (http://www.ezanalyze.com, Timothy Poynton, USA). A *P* value of <0.05 was considered significant. Continuous variables were expressed as mean and standard deviation. Categorical variables were expressed as percentages. To look at the association between 2 continuous variables, Pearson's correlation coefficient method was used. To compare means of 2 continuous variables, *t* test was used. To look at the association between 2 categorical variables, chi-square test was used.

Results

The mean age of the patients was 60.21 ± 10.74 years. There were 18 female patients and 43 male patients. Eleven patients (18.03%) had evidence of systolic dysfunction on echocardiography. At the end of one year, 38 patients had survived, 10 patients died, 3 patients were transferred to continuous ambulatory peritoneal dialysis, and 10 patients were transferred to other centers. All these patients were receiving erythropoiesis stimulating agents (ESA) on a regular basis.

There was a significant relationship between HbA1c and blood hemoglobin values using Pearson's correlation coefficient (r = 0.245, *P* = 0.05). Figure 1 shows the correlation between the two values.

Table 1 shows the clinical variables of the patients involved in the study. Table 2 shows the comparison of various parameters between those patients who survived and died at the end of 1 year. Table 3 shows the survival rates of patients with Hba1c levels ≤6%, 6%-8% and ≥8%. Figure 2 shows the comparison between survived and non-survived patients.

Table 1. Clinical variables of these patients

Variable	Mean value
Duration of haemodialysis (y)	2.60 ± 2.71
Hemoglobin A1c levels (%)	7.01 ± 1.66
Blood hemoglobin levels (g/dL)	9.08 ± 1.21
Systolic blood pressure (mm Hg)	156.75 ± 21.86
Diastolic blood pressure (mm Hg)	84.25 ± 11.85

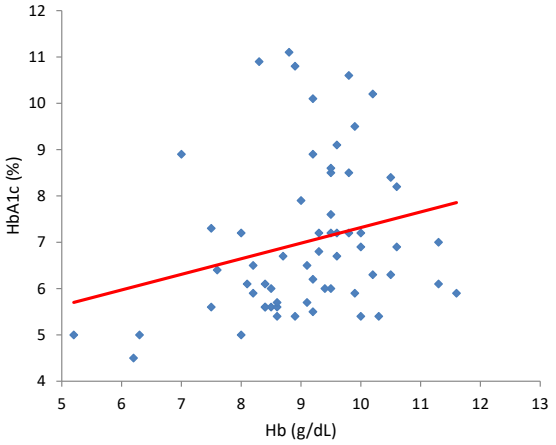

Figure 1. Scatter plot showing relationship between HbA1c and blood haemoglobin values (r = 0.245, *P* = 0.05).

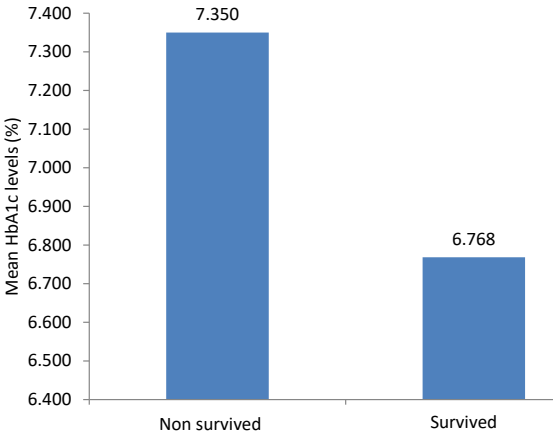

Figure 2. The comparison of HbA1c in the patients who survived and expired at the end of one year after the measurement (*P* = 0.326).

Discussion

In patients with advanced CKD, targeting a HbA1c of <7% may be associated with increased risk of developing hypoglycemia (5–7). HbA1c level is largely affected by glycemic status, acidosis, the degree of anemia and the RBC life span (1,2). Similar to the diabetic non-CKD population, high levels of HbA1c are strongly

Table 2. Comparison of parameters between survived and non-survived patients by independent samples *t* test

Variable	Survived patients (n=38)	Non-survived patients (n=10)	*P* value
Hemoglobin A1c (%)	6.768 ± 1.602	7.350 ± 1.834	0.326
Hemoglobin levels (g/dL)	9.003 ± 1.111	9.430 ± 0.975	0.274
Duration of dialysis (y)	3.347 ± 3.032	1.423 ± 1.401	0.058
Systolic blood pressure (mm Hg)	160.895 ±19.924	147.100 ± 20.599	0.059
Diastolic blood pressure (mm Hg)	84.263 ± 11.822	82.200 ± 9.151	0.611

Table 3. Comparison of survival rates of groups based on HbA1c values using chi-square test

HbA1c levels	≤6%	6.1%-7.9%	≥ 8%	P value
Survived	16 (84.2%)	16 (84.2%)	6 (60%)	0.245
Non- survived	3 (15.8%)	3 (15.8%)	4 (40%)	

associated with a high glycemic state and accompanying complications in dialysis patients (1). The association of higher HbA1c values with mortality in HD patients has been reported several times in the literature. A study of 54757 HD patients by Ricks et al, found that time-averaged HbA1c values >8% and <6% were associated with an increased mortality risk (8). Ramirez et al, also showed higher mortality rate in 9201 patients with a HbA1c <6% and ≥9% (10). A large prospective study of 24875 patients reported that intensity of glycemia represented by a HbA1c of ≤5% and >11% were associated with poor outcomes (9). This is the first study from India, looking at HbA1c values and mortality in Indian dialysis patients.

In our study of HbA1c of our diabetic dialysis population, there seems to be a trend for those patients who survived had a lower HbA1c value (mean = 6.768 ± 1.602%) despite having longer dialysis duration (3.347 ± 3.032 years). However, owing to small sample size, statistical significance could not be obtained. This is probably because of a higher proportion (40%) of non-survived patients in the group having >8% HbA1c. In our patients, HbA1c levels were directly correlated with blood hemoglobin levels. This is probably related to the lifespan of the red blood cells, which is often reduced in uremic patients (2,3). None of the patients had hemolytic anemia on assessment. About 60% of the deaths were due to cardiovascular disease, and the others died at home, so the cause of death is not known.

Conclusion

Diabetic patients have poor survival rates on hemodialysis compared with non-diabetic patients (13,14). This study shows poor glycemic control could be one of the factors that could be responsible for the poor survival rates in diabetic patients on hemodialysis. Larger prospective studies need to be done to establish this relationship.

Limitation of the study

The main limitations of this study are the small sample size, lack of serial measurements of HbA1c, which has been planned as an ongoing study.

Authors' contribution

GA, AKD and VM designed the project. SM collected the data. SN, RP, and MV analysed the data. MV and GA wrote the manuscript. DG, MM, AKD and VM edited the final draft. All authors and read and signed the final manuscript.

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest. The results presented in this paper have not been published previously in whole or part, except in abstract format.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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