Prevalence Of Glycemic Variability And Factors Associated With The Glycemic Arrays Among End-Stage Kidney Disease Patients On Chronic Haemodialysis.

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Abstract

Introduction: Glycaemic variability (GV) confers a significantly higher risk of diabetic-related complications, especially cardiovascular. Despite extensive research in this area, data on end-stage-kidney-disease (ESKD) patients on chronic haemodialysis are scarce. This study aims to determine the magnitude of GV among ESKD (diabetic vs non-diabetic) patients and its associated factors on haemodialysis days (HDD) and non-haemodialysis days (NHDD).

Methods: We recruited 150 patients on haemodialysis, 93 patients with diabetic (DM-ESKD), and 57 with non-diabetic (NDM-ESKD). The GV indices (standard deviation [SD] and percentage co-efficient variant [%CV]) were obtained from 11-point and 7-point self-monitoring blood glucose (SMBG) profiles on HDD and NHDD. The GV indices and its associated factors of both DM-ESKD and NDM-ESKD were analysed to compare HDD vs. NHDD.

Results: Mean blood glucose on HDD was 9.33 [SD 2.7, %CV 30.6%] mmol/L in DM-ESKD compared to 6.07 [SD 0.85, %CV 21.3%] mmol/L in NDM-ESKD (p =<0.01). The DM-ESKD group experienced significantly higher GV indices compared to NDM-ESKD on both HDD and NHDD, particularly in the subgroup with HbA1c 8-10% (p =<0.01). Presence of diabetes, older age, hyperlipidaemia, HbA1c, ferritin levels, and albumin were identified as factors associated with GV.

Conclusion: DM-ESKD patients have high GV, especially on HDD, therefore increasing their risk of developing future complications. We identified high HbA1c, older age group, presence of hyperlipidaemia, ferritin levels, and albumin as factors associated with GV. Since these groups of patients are vulnerable to CVD mortality, urgent attention is needed to rectify it.

Background

Type 2 Diabetes Mellitus (T2DM) is the primary cause of end-stage-kidney-disease (ESKD) worldwide [1, 2]. A similar trend is seen in Malaysia, where the prevalence of ESKD has doubled over the last ten years, with almost two-thirds of patients having diabetes [3]. Diabetic ESKD (DM-ESKD) is associated with higher morbidity and mortality, mainly related to cardiovascular complications, with poor glycemic control proven to be a predictor of mortality [4]. Therefore, glycemic control had been a focus of extensive research, especially among DM-ESKD on haemodialysis, as these patients experience more marked fluctuations in blood glucose compared to non-haemodialysis diabetic populations [5].

Glycemic variability (GV) had been coined to explain these glucose fluctuations among diabetic patients. GV has been shown to be an independent risk factor for morbidity and mortality among the non-haemodialysis diabetic population as previous studies have demonstrated failure in improving cardiovascular outcomes by targeting HbA1c alone, a surrogate for chronic hyperglycaemia[6–9].

Data from the general population had prompted concerns regarding glycemic control among ESKD patients that have higher cardiovascular risk. Large population studies among haemodialysis patients have shown an association between HbA1c levels of less than 6% and more than 8% with decreased overall survival [10, 11]. This U-shape association in haemodialysis patients might indicate that chronic hyperglycemia per se is not an
indicator of morbidity and mortality, but also hypoglycemia with glucose fluctuations that were more evident in these malnourished and protein-energy wasted patients [5, 11].

These findings indicate that reducing GV may be an important strategy in reducing cardiovascular complications in the haemodialysis population. However, although GV has been heavily investigated in non-ESKD diabetic patients, minimal data is available in ESKD patients, especially on the extent of GV on haemodialysis (HDD) and non-haemodialysis days (NHDD). Furthermore, data on GV still lacks among the Malaysian population. We conducted a previous analysis of glycemic patterns during haemodialysis in our population, showing that DM-ESKD patients experience four times more post-haemodialysis hyperglycemia compared to their non-diabetic counterparts [12]. Therefore the objectives of this study are to determine further the magnitude of GV and its associated factors among ESKD patients on HDD and NHDD to optimise management in this patient group.

**Methods**

**Study design**

In this cross-sectional study, we recruited 150 ESKD patients on maintenance haemodialysis with DM-ESKD (n=93) and NDM-ESKD (n=57). This study was approved by the ethical committee of University Putra Malaysia (UPM) and was conducted according to the Declaration of Helsinki, where written consent was obtained prior to study participation. Patients were recruited from 5 private haemodialysis centres in Selangor, Malaysia. The sample size was calculated based on a study by Jin Y.P, 2015, which looked at blood glucose fluctuations among haemodialysis population [13]. Multiple logistic regression using G power software [14] was used by considering a model with one binary covariate X with event rate under Ho, p$_1$ = 0.13 and event rate under X = 1, p$_2$ = 0.40, giving an odds ratio of ~ 4.5. We further assumed R$^2$ = 0.1, and an imbalanced design ratio of 2:1 between the two groups. The estimated sample size necessary to achieve a two-sided test with an alpha of 0.05 and power of at least 80% was 102. The final sample size was 146 rounded to 150, considering a 30% non-response rate.

Inclusion criteria were: adults over 18 years of age with or without diabetes, patients on maintenance haemodialysis for at least three months, patients with stable haemoglobin levels over the last three months and patients with no recent change in insulin or oral hypoglycemic agents. Exclusion criteria were: Type 1 diabetes mellitus, blood transfusion or hospitalisation within the previous three months, hemoglobinopathy, presence of acute inflammatory state, and diagnosis of malignancy.

**Socio-demographic and comorbidity data**

A structured questionnaire was developed for socio-demographic information, medical information, comorbidities and prescription lists. Baseline blood tests were taken from patients at the start of the study. All blood specimens were processed in the same laboratory for uniformity.

**Haemodialysis day**

SMBG was done on two consecutive days (HDD and NHDD). Patients’ haemodialysis regimens were as prescribed by their nephrologists and not altered for the study. Monitoring of clinical parameters was performed
according to standard of care.

**Self Monitoring of Blood Glucose**

Capillary glucose measurement was measured using standardised capillary glucometers (Bayer contour plus®) in this study. Patients were trained to measure capillary glucose and to record glucose values. They were also taught to recognise symptoms of hypoglycemia and to record their blood glucose if they occurred.

On HDD, an 11-point capillary self-monitoring blood glucose (SMBG) profile was obtained: fasting, pre-haemodialysis, hourly during haemodialysis, followed by pre-and post-meal glucose readings at home. During haemodialysis, patients were assisted in the measurement of blood glucose levels. On NHDD, a 7-point SMBG profile was measured: fasting, pre- and post-meal for breakfast, lunch and dinner. Patients were advised to continue taking their usual medications, either on HDD or NHDD. Patients were not required to fast during haemodialysis. They were advised to eat as usual and log all meals and snacks.

**Assessment of Glycemic variability (GV)**

We chose standard deviation (SD) and percentage co-efficient (%CV) as indices of GV, calculating these from SMBG reading on HDD and NHDD days. The SD was calculated as arithmetic SD, and %CV was obtained by \((\text{SD of glucose}/\text{mean glucose}) \times 100\). Ideal target GV was calculated as follows: \(\text{SD} \times 3 < \text{mean glucose}\) and for %CV the value of \(< 36\% \) [15, 16].

**Statistical analysis**

Statistical analysis was performed using RStudio. GV was calculated using two methods, i.e. SD and %CV. The data was checked for normality visually using a histogram and statistically using the Shapiro Wilk test. For univariate analysis, the chi-square test and independent-sample t-test were used. The assumption for equal variance was met using Levene's test. All tests were two-sided, and the level of significance was set at 0.05. The association between GV with clinical and laboratory results were determined using simple logistic regression to derived crude odds ratios. Subsequently, variables which were significant at \(p < 0.15\) were included in the final multivariable logistic regression analysis. All crude and adjusted odds ratios were presented with 95% confidence intervals. For missing data, the listwise deletion method was used.

**Results**

**Baseline socio-demographic, clinical characteristics and blood parameters of patients**

The summary of baseline socio-demographic, clinical characteristics, and blood parameters of patients are shown in Table 1 [12]. A total of 148 patients were involved in the final analysis after excluding missing data. DM-ESKD accounted for 91 (61.5%) of patients with a mean age of 57.6 years and a mean duration of diabetes of 16.4 years. The mean duration of haemodialysis between DM-ESKD and NDM-ESKD was 3.8 and 4.5 years, respectively, and not statistically significant. A quarter of the patients reported a history of ischaemic heart disease, however, the difference in the prevalence of cardiovascular disease in both groups was not statistically significant.
Table 2 shows the types of medications prescribed in our study population. Antihypertensive agents were prescribed in 89 (60.1%) of patients; however, blood pressure control in both groups were suboptimal with only 16 (10.7%) of DM-ESKD and 47 (31.3%) of NDM-ESKD patients achieving pre and post haemodialysis target blood pressure of less or equal to 130/80 mmHg. Among DM-ESKD patients, 50 (54.9%) were on insulin therapy and a quarter not on pharmacological treatment. The mean HbA1c among DM-ESKD patients was 7.4%, with around one-third having HbA1c less than 6.5% while another 30% of patients had HbA1c in the range of 6.5% to 8%. Medication intake on HDD depended on the type of treatment: as per usual practice in the haemodialysis centers, i.e., patients on OHA alone would not take their OHA on HDD, while patients on basal-bolus insulin would omit the insulin dose before their haemodialysis session. However, the majority of patients, i.e. 56 (82.3%) patients, would not take their medications on HDD. Statins were prescribed in 66 (44.6%) of patients with a mean LDL of 2.97 mmol/L and 3.17 mmol/L in DM-ESKD and NDM-ESKD, respectively. Almost half of the patients were on iron supplementation, either oral or intermittent intravenous iron preparation, and almost all of the patients were on erythropoietin. The mean value of ferritin levels was 554.1 ug/L and 665.2 ug/L in DM-ESKD and NDM-ESKD, respectively.

In general, both groups had a statistically non-significant difference in terms of blood parameters (Table 1) apart from HbA1c, phosphate, and albumin. Albumin was lower in the DM-ESKD group, while phosphate is higher in NDM-ESKD. Highly sensitive C-reactive protein (hs-CRP) was used as a surrogate marker for cardiovascular risk, and both groups had a high hs-CRP level with a mean of 8.91mg/L in and 7.03 in DM-ESKD and NDM-ESKD respectively.

GV among ESKD patients

GV on HDD

Mean blood glucose ± SD during haemodialysis among DM-ESKD and NDM-ESKD in our study was 9.33 ± 2.7 mmol/L vs. 6.07 ± 0.85 mmol, respectively. Table 3 compares the GV indices between DM-ESKD and NDM-ESKD patients during HDD and NHDD. The majority of our patients achieved target GV i.e. 111 (75.0%), based on SD and 121 (81.8%) based on %CV with higher mean GV for DM-ESKD [SD: 2.7; %CV: 30.6%] compared to NDM-ESKD [SD: 0.85, %CoV: 21.3%; p <0.01]. DM-ESKD had higher prevalence of high GV compared to NDM-ESKD [SD: 33.0%, %CV: 25.3% vs. SD: 12.2%, %CV:7.1%]. HDD GV indices were the highest in Hba1c group 8-10% and lowest in the < 6.5%. Figure 1 represents the glycemic patterns based on GV indices on HDD.

GV on NHDD

On NHDD, the mean blood glucose ± SD among DM-ESKD and NDM-ESKD was 9.85 ± 3.1 mmol/L vs. 6.0 ± 0.88 mmol, respectively. Mean GV for DM-ESKD was higher [SD: 3.1; %CV: 22.9%] compared to NDM-ESKD [SD: 0.88, %CV: 15.1%; p < 0.01] with 12.1% (SD) and 8.8% (%CV) of DM-ESKD experienced high GV. None of the NDM-ESKD patients demonstrated high GV indices during NHDD. GV indices were lowest among patients with HbA1c <6.5%, while highest among those with HbA1c 8-10%. Figure 2 represents the glycemic patterns based on GV indices on NHDD.

GV HDD and NHDD
Significantly more patients achieved target GV on NHDD days as compared to HDD (SD: 75.0% vs 92.6%; %CV: 82.0% vs 92.7%). However, when we factor in diabetes status, the results were not statistically significant (Table 4).

Factors associated with high GV among ESKD patients

Tables 5 and 6 demonstrate the association between clinical characteristics and blood parameters with GV on HD and NHDD. In this study, the presence of diabetes and older age was associated with high GV. While the additional presence of hyperlipidemia was associated with higher GV on NHDD. HbA1c, ferritin, LDL, and TG were associated with high GV during haemodialysis day. On NHDD, HbA1c, albumin, and ferritin were associated with high GV. Further multivariate analysis (Table 7 and 8) showed that age and LDL were factors associated with GV on HDD while albumin was associated with high GV on NHDD. There was no association between type of medications with GV (Table 9). We found a weak and non-significant linear correlation between serum albumin and LDL level ($r (147) = 0.08, p = 0.34$) and between serum ferritin and HSCRP level ($r (147) = -0.07, p = 0.41$).

Discussion

Dysglycemia in diabetes mellitus consists of three main components: sustained chronic hyperglycemia, GV, and hypoglycemic episodes, with each component appearing to be a link in a chain for the development and progression of diabetes-related complications [17]. Previous studies have shown that besides HbA1c, short-term daily GV represents an independent risk factor for diabetes complications [18, 19]. Furthermore, haemodialysis is another independent risk factor for GV [20]. Hence, it is paramount important to evaluate the GV among ESKD patients as they are more vulnerable to cardiovascular complications.

GV denotes swings in blood glucose level that occur throughout the day, including hypoglycemic periods, post-prandial increases, and other blood glucose fluctuations that occur at the same time on a different day [21]. In our previous study, we noted that DM-ESKD patients experienced greater fluctuations in blood glucose and had a fourfold increase in post-prandial blood glucose compared to NDM-ESKD [12]. We also noted episodes of intra-dialytic asymptomatic hypoglycemia in 12% of both DM-ESKD and NDM-ESKD patients, which demonstrated that blood glucose fluctuation occurs in all haemodialysis patients regardless of the presence of diabetes [12]. In our current study, GV among ESKD patients on haemodialysis was generally acceptable, where up to 80% and 90% of patients achieved the target GV on HDD and NHDD, respectively. We observed marked GV differences between our DM-ESKD patients with up to 33% experiencing high GV compared to NDM-ESKD (up to 12%) on HDD, which persists to NHDD (Figures 1 & 2). Interestingly, despite the absence of T2DM, a small percentage of NDM-ESKD experienced high GV on HDD with none of them showing high GV on NHDD. This observation supports the notion that haemodialysis is an independent risk factor for GV even among NDM-ESKD patients. Our findings correlate with other studies, which also show worsened glycaemic control among haemodialysis patients and larger GV among diabetic compared to non-diabetic patients (Table 10) [13, 20, 22–25].

Although we observed a higher GV among DM-ESKD with HbA1c 8-10%, the sole use of HbA1c in ESKD is limited by several factors, e.g., anaemia, uremia, acidosis, and malnutrition [26]. In the general population, there is a linear relationship between HbA1c and mean blood glucose with $R^2$ more than 0.80, which makes HbA1c
as an excellent surrogate marker for glycaemic control [27]. In our study, the relationships between mean blood glucose and HbA1c were moderate, with $R^2 = 0.59$ [12]. Our result was similar to bigger studies among haemodialysis patients, where the relationship ($R^2$) is not more than 0.50 [28]. Therefore, knowledge of factors associated with GV apart from HbA1c as a surrogate marker is essential as it allows health professionals to provide targeted interventions to patients with a higher risk of diabetic complications. Currently, many studies that investigate factors affecting GV were done amongst diabetic patients with normal renal function. Moreover, results from these studies varied among each other with small sample size and different indexes of measuring GV [29–38].

We found that GV is higher in patients with older age, DM-ESKD, and hyperlipidemia. Blood parameters associated with high GV were HbA1c, ferritin level, lipid profile, and albumin. HbA1c and its association with GV and mean blood glucose among patients had been heavily investigated with inconsistent results. In our study, HbA1c, especially levels between 8 and 10%, was associated with higher GV. Current literature on the association of HbA1c with GV is heterogeneous, with results showing a weak correlation between HbA1c and GV but had a significant association with chronic hyperglycemia and average blood glucose [29, 30, 32, 33]. Conversely, recent studies among Asian populations, showed similar findings with our study where HbA1c correlates well with GV indices [34, 35]. However, most of these studies include only patients with normal renal function in whom HbA1c is more reliable as a surrogate marker and would not be affected by the anaemia commonly seen in ESKD patients.

GV may be related to pancreatic beta-cell dysfunction and insulin resistance, which may occur part of the aging process and duration of T2DM. In our study, older age was associated with higher GV, which corroborates a previous Asian study that showed an association of GV with older age, longer duration of diabetes, and low c-peptide [34, 35]. Types of medication also may reflect the process of pancreatic beta-cell dysfunction. Although no association between GV with types of medication was found in this study, previous studies showed an association between the use of insulin and sulfonylureas (insulin secretagogues) with higher GV [31, 37, 38]. In T2DM, beta-cell dysfunction plays a significant role in dysglycaemia, where insufficient insulin secretion for accurate regulation may lead to glucose-related metabolic disorders, exposing patients to increased GV and sustained hyperglycemia [39–41]. Furthermore, aging alone significantly affects pancreatic B cells due to deterioration in secretory and regenerative capacity [42, 43].

Hyperlipidaemia is recognized as a risk factor for IHD and coronary mortality and was associated with high GV in our study [44, 45]. High-sensitive C-reactive protein (hs-CRP) was used to estimate cardiovascular risk in our population, and although it did not have a significant association with GV, we found that both DM-ESKD and NDM-ESKD patients had higher hs-CRP levels with a mean of 8.91 mg/L and 7.03 mg/L respectively [12]. GV may further increase cardiovascular risk by propagating oxidative stress, leading to endothelial dysfunction and angiopathies [46]. In our study, higher ferritin, although a non-specific inflammatory marker, was seen more frequently in the target GV group compared to the high GV group. Nonetheless, patients with high GV also demonstrate high ferritin level with a mean value 554.1 ug/L. Although a significant number of our patients were on iron supplementation, we found the level of ferritin is independent of hs-CRP, a better marker for inflammation in cardiovascular disease. High ferritin and quantitative C-reactive protein levels have been associated with accelerated atherosclerosis in ESKD patients; however, it is unclear to us whether ferritin levels can be reliably interpreted in patients on iron supplementation [47]. A study using a more specific marker for
oxidative stress, N, N-diethyl paraphenylenediamine, showed an association between high GV and high oxidative stress [48]. In our cohort, the albumin level was lower among DM-ESKD as compared to NDM-ESKD and was associated with high GV. LDL, although not a significant factor for GV was also lower in DM-ESKD, which may represent nutritional status among diabetic patients. Notably, it had a poor correlation with albumin in our study. A 10-year cohort study evaluated serum albumin, C-reactive protein, and carotid atherosclerosis as predictors of 10-year mortality in haemodialysis patients showed that serum albumin concentration was a better predictor of mortality [50]. Hence, targeting chronic inflammation and improving nutrition, and observing the effect on GV could be a subject for future research.

The limitations of our study are the cross-sectional design, utilisation of SMBG instead of continuous glucose monitoring, which is more accurate in assessing GV, and possibly the lack of standardised dietary restriction in our patients. We elected for SMBG due to ease of availability and lower cost, which makes it the preferred method for glucose monitoring in our population. We did not limit or measure the dietary intake of the patients during the study period, which may make it a confounding factor in the glycaemic profile of the patients. Some previous studies restricted dietary intake or mandated fasting during HD, however, the readings would not be representative of normal day-to-day glucose fluctuations. Therefore by allowing usual dietary intake, it would be more practical, reflective of real-life data, and may subsequently allow alterations in management.

**Conclusion**

ESKD patients experienced significant GV on HDD and NHDD with a more pronounced effect seen among DM-ESKD patients. High GV was associated with older age, DM-ESKD, hyperlipidemia, high HbA1c, ferritin, and albumin. These factors correlate to the progression of the illness, beta-cells dysfunctions, and chronic malnutrition-inflammatory state seen among ESKD patients. Regular glucose monitoring, in particular on HDD may be beneficial in these groups of patients to optimise management and to reduce diabetic-related complications.

**Abbreviations**

ALP = Alkaline phosphatase

BMI = Body mass index

CGMS = continuous glucose monitoring system

DM-ESKD = Diabetic End-Stage-Kidney-Disease

ESKD = End-Stage-Kidney-Disease

GV = Glycemic variability

HbA1c = Hemoglobin A1c

HB = hemoglobin

HDD = Haemodialysis day
HDL = High density lipoprotein
Hs-CRP = Highly sensitive C-reactive protein
IHD = Ischemic heart disease
iPTH = Intact parathyroid hormone
LDL = low density lipoprotein;
MAGE = Mean Amplitude Of Glycaemic Excursion
NDM-ESKD = Non-diabetic End-Stage-Kidney-Disease
NHDD = Non-Haemodialysis day
SD = Standard deviation
SMBG = Self-monitoring blood glucose
TG = triglycerides
T2DM = Type 2 Diabetes Mellitus
% CV = percentage co-efficient variant

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by University Putra Malaysia Ethics Committee involving human (UPM/TNCPI/RMC/1.4.18.2/JKEUPM), and was carried out in accordance with the principles of the Declaration of Helsinki.

CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

No conflict of interest.

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AUTHORS’ CONTRIBUTION
All authors have read and approved the manuscript.

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AVAILABILITY OF DATA AND MATERIAL

The datasets used during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1
Baseline sociodemographic, clinical characteristics and blood parameters of patients. (n = 148)
| Characteristics | DM-ESKD | NDM-ESKD | Test statistic | P-value |
|-----------------|---------|----------|----------------|---------|
| **Mean (SD)**   |         |          |                |         |
| Age (years)     | 57.6 (11.1) | 49.0 (11.2) | -4.590         | <0.001*** |
| Duration of HD (years) | 3.8 (3.1) | 4.5 (3.3) | 1.310 | 0.198 |
| BMI (kg/m²)     | 27.1 (4.4) | 26.2 (6.6) | -0.862 | 0.391 |
| **n (%)**       |         |          |                |         |
| Sex             |         |          |                |         |
| Male            | 51 (56.0) | 30 (52.6) | 0.165 | 0.685 |
| Female          | 40 (44.0) | 27 (47.4) | 1.078 | 0.583 |
| Race            |         |          |                |         |
| Malay           | 79 (86.8) | 52 (91.2) | 10.729 | 0.030*** |
| Chinese         | 1 (1.1) | 1 (1.8) | 10.729 | 0.030*** |
| Indian          | 11 (12.8) | 4 (7.0) | 0.165 | 0.685 |
| BMI             |         |          |                |         |
| Underweight (<18.5) | 1 (1.1) | 4 (7.0) | 0.165 | 0.685 |
| Normal (18.5-22.9) | 11 (12.8) | 15 (26.3) | 1.078 | 0.583 |
| Overweight (23.0 - 24.9) | 15 (16.5) | 7 (12.3) | 1.078 | 0.583 |
| Obese Class 1 (25.0 - 29.9) | 41 (45.1) | 16 (28.1) | 0.030*** | 0.030*** |
| Obese Class 2 (>30.0) | 11 (12.8) | 4 (7.0) | 0.165 | 0.685 |
| BP Target Pre HD |         |          |                |         |
| Pre-HD BP (≤130/80) | 12 (13.2) | 4 (7.0) | 1.383 | 0.240 |
| Pre-HD BP (>130/80) | 79 (86.8) | 53 (93.0) | 1.383 | 0.240 |
| BP Target Pre HD |         |          |                |         |
| Post HD BP (≤130/80) | 34 (37.4) | 13 (22.8) | 3.426 | 0.064 |
| Post HD BP (>130/80) | 57 (62.6) | 44 (77.2) | 3.426 | 0.064 |
| Smoking         |         |          |                |         |
| Yes             | 4 (4.4) | 10 (17.5) | 7.074 | 0.008*** |
| No              | 87 (95.6) | 47 (82.5) | 7.074 | 0.008*** |
| Hypertension    |         |          |                |         |
| Yes             | 90 (98.9) | 54 (94.7) | 2.311 | 0.128 |
| No              | 1 (1.1) | 3 (5.3) | 2.311 | 0.128 |
| IHD             |         |          |                |         |
| Yes             | 26 (28.6) | 12 (21.1) | 1.038 | 0.308 |
| No              | 65 (71.4) | 45 (78.9) | 1.038 | 0.308 |
| Gout            |         |          |                |         |
| Yes             | 6 (6.6) | 7 (12.3) | 1.415 | 0.234 |
| No              | 85 (93.4) | 50 (87.7) | 1.415 | 0.234 |
| Stroke          |         |          |                |         |
| Yes             | 5 (5.5) | 2 (3.5) | 0.307 | 0.580 |
| No              | 86 (94.5) | 55 (96.5) | 0.307 | 0.580 |
| Hyperlipidaemia |         |          |                |         |
| Yes             | 56 (61.5) | 27 (47.4) | 2.857 | 0.091 |
| No              | 35 (38.5) | 30 (52.6) | 2.857 | 0.091 |
| **Blood Parameters** |        |          |                |         |
| Hemoglobin (g/dL) | 10.47 (1.7) | 10.38 (1.7) | -0.339 | 0.735 |
| HbA1c (%)       | 7.40 (1.6) | 5.41 (0.5) | -10.845 | <0.001*** |
| Total cholesterol (mmol/L) | 4.8 (1.3) | 5.0 (1.2) | 1.003 | 0.318 |
| Parameter                  | Mean ± SD     | Mean ± SD     | Mean ± SD     | Mean ± SD     |
|---------------------------|---------------|---------------|---------------|---------------|
| LDL (mmol/L)              | 2.97 (1.16)   | 3.10 (1.18)   | 0.664         | 0.508         |
| TG (mmol/L)               | 2.30 (1.7)    | 2.04 (1.4)    | -1.030        | 0.304         |
| HDL (mmol/L)              | 2.97 (0.22)   | 1.08 (0.29)   | 2.560         | 0.012         |
| HSCRP (mg/L)              | 8.91 (10.2)   | 7.03 (7.1)    | -1.310        | 0.192         |
| Ferritin (ug/L)           | 554.1 (402)   | 665.2 (435)   | 1.497         | 0.137         |
| Transferrin saturation (%)| 23.96 (11.2)  | 24.82 (8.8)   | 0.526         | 0.600         |
| Calcium (mmol/L)          | 2.16 (0.22)   | 2.19 (0.24)   | 0.883         | 0.379         |
| Phosphate (mmol/L)        | 1.85 (0.54)   | 2.18 (0.73)   | 2.893         | 0.005***      |
| iPTH (pmol/L)             | 73.6 (58.3)   | 103.7 (105.1) | 1.889         | 0.063         |
| ALP (U/L)                 | 176.32 (173.3)| 143.37 (112.2)| -1.413        | 0.159         |
| Albumin (mmol/L)          | 38.3 (4.2)    | 40.1 (2.7)    | 3.190         | 0.002***      |

The baseline sociodemographic, clinical characteristics and blood parameters of patients (n=148), values expressed as mean ± standard deviation. DM-ESKD, diabetic-end stage kidney disease; NDM-ESKN, non-diabetic end-stage-kidney-disease; HD, hemodialysis; BMI, body mass index, HbA1c, glyclated hemoglobin; LDL, low density lipoprotein; TG, triglycerides; HDL, high density lipoprotein; HSCRP, highly sensitive C-reactive protein; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase.*Independent t-test **Chi-square test ***P value<0.05. [12]

Table 2
Type of medication prescribed to patients in the study (n = 148)
| Type of medication                                      | n (%)  |
|--------------------------------------------------------|--------|
| Antidiabetics agents (DM-ESKD, n= 91)                  |        |
| · Insulin basal bolus                                   | 27 (29.7) |
| · Insulin premixed                                      | 23 (25.3) |
| · Insulin basal and oral hypoglycemic agent (OHA)       | 2 (2.2)  |
| · Oral hypoglycemic agent (OHA)                         | 16 (17.6) |
| · No medication                                         | 23 (25.3) |
| Anti- Hypertensive agent                                |        |
| Anti-platelet                                           | 89 (60.1) |
| Statin                                                  |        |
| Phosphate binders                                       | 41 (27.7) |
| Vitamin D                                               | 66 (44.6) |
| Diuretics                                               |        |
| Iron supplements (oral or injectable)                   | 146 (98.6) |
| Erythropoietin (EPO)                                    |        |
| No                                                      | 76 (51.4) |
| 2000                                                    | 49 (33.1) |
| 4000                                                    | 17 (11.5) |
| 6000                                                    | 21 (14.2) |
| 8000                                                    | 20 (13.5) |
| 12000                                                   | 5 (3.4)  |

The type of medications prescribed to the patients in the study (n=148), values expressed as number and percentage.

**Table 3**
Comparison of GV indices between DM-ESKD and NDM-ESKD during haemodialysis and non-haemodialysis day.
Glycaemic variability (GV) indices (SD, standard deviation; %CV, percentage co-efficient variant) among all patients and also comparing DM-ESKD and NDM-ESKD during haemodialysis day (HDD) and non-haemodialysis day (NHDD) (student t-test). The results showed in the number (n) and percentage. * p < 0.05.

| GV indices | All patients, n (%) | DM-ESKD, n (%) | NDM-ESKD, n (%) | t statistic | p-value |
|------------|---------------------|----------------|----------------|-------------|--------|
| HDD        |                     |                |                |             |        |
| SD         |                     |                |                |             |        |
| Target GV: (<mean/3) | 111 (75.0) | 61 (67.0) | 50 (87.7) | 8.700 | 0.003* |
| High GV: (>mean/3)  | 37 (25.0) | 30 (33.0) | 7 (12.2) | 8.726 | 0.003* |
| %CV        |                     |                |                |             |        |
| Target GV: <36%  | 121 (81.8) | 68 (74.7) | 53 (92.9) | 8.726 | 0.003* |
| High GV: > 36%   | 27 (18.2) | 23 (25.3) | 4 (7.1) | 8.726 | 0.003* |
| NHDD        |                     |                |                |             |        |
| SD         |                     |                |                |             |        |
| Target GV: (<mean/3) | 137 (92.6) | 80 (87.9) | 57 (100) | 6.649 | 0.009* |
| High GV: (>mean/3)  | 11 (7.4) | 11 (12.1) | 0 (0) | 6.649 | 0.009* |
| %CV        |                     |                |                |             |        |
| Target GV: <36%  | 139 (93.9) | 83 (91.2) | 57 (100) | 4.545 | 0.033* |
| High GV: > 36%   | 8 (6.1) | 8 (8.8) | 0 (0) | 4.545 | 0.033* |

Table 4
Comparison of GV indices between haemodialysis and non-haemodialysis day

| SD                  | Proportion of target | c statistic | p-value |
|---------------------|----------------------|-------------|---------|
|                     | HDD, n (%)           | NHDD, n (%) |         |
| All Patients        | 111 (75.0)           | 137 (92.6)  | 16.499  | <0.001* |
| DM-ESKD             | 61 (67.7)            | 80 (56.3)   | 0.25    | 0.6171  |
| NDM-ESKD            | 50 (46.8)            | 57 (53.2)   | 0.25    | 0.6171  |

| % CV                | Proportion of target | c statistic | p-value |
|---------------------|----------------------|-------------|---------|
|                     | HDD, n (%)           | NHDD, n (%) |         |
| All Patients        | 121 (82.0)           | 137 (92.7)  | 11.316  | <0.001* |
| DM-ESKD             | 68 (41.4)            | 83 (58.6)   | 1.132   | 0.2874  |
| NDM-ESKD            | 53 (48.2)            | 57 (51.8)   | 1.132   | 0.2874  |

Glycaemic variability (GV) indices (SD, standard deviation; %CV, percentage co-efficient variant) among all patients and also comparing haemodialysis (HDD) and non-haemodialysis day (NHDD) (chi-square analysis). The result is
shown in number (n) and percentage. * p < 0.05. DM-ESKD, diabetic-end stage renal disease; NDM-ESKD, non-diabetic end-stage-renal-disease.

Table 5.
Factors associated with poor GV during haemodialysis day using simple logistic regression.
|                             | SD         | Test statistic | p-value | Crude Odds ratio (95% CI) | % CV | Test statistic | p-value | Crude Odds ratio (95% CI) |
|-----------------------------|------------|---------------|---------|---------------------------|------|---------------|---------|---------------------------|
| **Diabetes**                |            |               |         |                           |      |               |         |                           |
| No                          | 50         |               | <0.01*  | Reference                 |      | 53            | 3       | Reference                 |
| Yes                         | (45.0, 17.1)| 3.96          | (43.8, 12.0) | (1.62, 11.25) | 68 | (56.2, 88.0) | 22 | (5.72, 1.85, 25.06) |
| **Gender**                  |            |               |         |                           |      |               |         |                           |
| Male                        | 59         |               | -0.413  | Reference                 |      | 65            | 14      | Reference                 |
| Female                      | (53.2, 57.1)| 0.85          | (53.7, 56.0) | (0.39, 1.82) | 56 | (46.3, 44.0) | 11 | (0.91, (0.38, 2.16)) |
| **Smoking**                 |            |               |         |                           |      |               |         |                           |
| No                          | 100        |               | -1.241  | Reference                 |      | 109           | 25      | Reference                 |
| Yes                         | (90.1, 97.1)| 0.267         | (90.1, 100.0) | (0.01, 1.45) | 12 | (9.9, 9) | 0.03* | (0.17, 0.01, 3.00) |
| **BMI**                     |            |               |         |                           |      |               |         |                           |
| Normal (18.5-22.9)          | 5 (4.5)    | -0.015        | 0.99    | Reference                 |      | 5 (4.1)       | 0 (0)   | Reference                 |
| Underweight (<18.5)         | 19         | 0.94          | 0.35    | 4.2 (0.2, 20)             | 6   | 0.81          | 0.42    | 3.5 (0.17, 72.00)         |
| Overweight                  | 17         | 0.94          | 0.35    | 2.8 (0.1, 18)             | 3   | 0.75          | 0.46    | 2.1 (0.09, 46.80)         |
| Obese 1 (25.0 - 29.9)       | 41         | 0.83          | 0.41    | 61.2 (14.9, 20)           | 12  | 0.231         | 0.82    | 46.80                     |
| Obese 2 (>30.0)             | 29         | 3.5           | 0.18    | 70.2 (28.1, 36.0)         | 4   | 1.4           | 0.07    | 30.50                     |
| **IHD**                     |            |               |         |                           |      |               |         |                           |
| No                          | 86         |               | -0.605  | Reference                 |      | 93            | 16      | Reference                 |
| Yes                         | (77.5, 65.7)| 1.79          | (76.9, 64.0) | (0.77, 4.08) | 28 | (23.1, 36.0) | 9  | (0.72, 4.63) |
| **Gout**                    |            |               |         |                           |      |               |         |                           |
| No                          | 100        |               | -0.75   | Reference                 |      | 110           | 23      | Reference                 |
| Yes                         | (90.1, 94.3)| 0.55          | (90.9, 92.0) | (0.08, 2.19) | 11 | (9.1) | 2 (0.8) | (0.13, 3.53) |
| **Hyperlipidaemia**         |            |               |         |                           |      |               |         |                           |
| No                          | 52         |               | 1.004   | Reference                 |      | 54            | 11      | Reference                 |
| Yes                         | (46.8, 37.1)| 1.49          | (44.6, 44.0) | (0.69, 3.32) | 67 | (55.4, 56.0) | 14 | (1.02, 0.43, 2.49) |
| **Stroke**                  |            |               |         |                           |      |               |         |                           |
| No                          | 105        |               | -0.605  | Reference                 |      | 114           | 25      | Reference                 |
| Yes                         | (94.6, 97.1)| 0.51          | (94.2, 100) | (0.03, 3.16) | 7  | (5.8, 0) | 0 (100) | (0.30, 0.17, 5.40) |
| **Hypertension**            |            |               |         |                           |      |               |         |                           |
| No                          | 4          |               | 0.725   | Reference                 |      | 4             | 0 (0)   | Reference                 |
| Yes                         | (3.6, 0)   | 3.00 (0.16, 117) | (3.3, 0) | (56.6, 96.7) | 25 | (9.0) | 0.63 | (1.02, 0.96, 1.07) |
| **Mean (SD)**               |            |               |         |                           |      |               |         |                           |
| Age                         | 53.1       | 2.236         | 0.03*   | 53.1                      | 58.4 | 3.06 | <0.01* | 1.07 |
| Duration HD                 | 4.1        | -0.0237       | 0.81    | 4.1                       | 4.0  | -0.215 | 0.83 | 0.99 (0.85, 1.12) |
| BMI (kg/m²)                 | 26.7       | 0.365         | 0.72    | 26.7                      | 27.1 | -0.727 | 0.47 | 0.97 (0.89, 1.05) |
| Hba1c                       | 6.4        | 3.030         | <0.01*  | 6.4                       | 7.4  | 1.664 | 0.10* | 1.23 (0.96, 1.57) |
| Hscrp                        | 7.3        | 1.11          | 0.27    | 7.3                       | 9.0  | 0.63  | 0.53 | 1.02 (0.96, 1.07) |
| Ferritin                    | 632.9      | -1.6          | 0.11*   | 632.9                     | 498.6 | -1.765 | 0.08* | 0.99 (0.99, 1.07) |

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Table 5 is a simple logistic regression analysis of sociodemographic, clinical comorbidities and blood parameters among patients in cohort (n=150) with poor GV during haemodialysis day.

*Factor significant at $P<0.15$ to be included in multiple logistic regression.

| Albumin | Clearance | LDL | HDL | HB | TG | Transferrin saturation | Calcium | Phosphate | ALP | iPTH |
|---------|-----------|-----|-----|----|----|------------------------|---------|-----------|-----|------|
| 38.9 (3.9) | 38.9 (3.4) | 0.132 | 0.90 | 1.01 (0.91,1.12) | 0.76 (0.53,1.08) | 0.14* (0.05,1.08) | 3.1 (1.1) | 2.7 (1.2) | 1.01 (0.97,1.07) | 0.72 (0.47,1.08) |
| 38.9 (3.4) | 38.9 (3.4) | 0.132 | 0.90 | 1.01 (0.91,1.12) | 0.76 (0.53,1.08) | 0.14* (0.05,1.08) | 3.1 (1.1) | 2.7 (1.2) | 1.01 (0.97,1.07) | 0.72 (0.47,1.08) |
| 0.132 | 0.90 | 1.01 (0.91,1.12) | 0.76 (0.53,1.08) | 0.14* (0.05,1.08) | 3.1 (1.1) | 2.7 (1.2) | 1.01 (0.97,1.07) | 0.72 (0.47,1.08) |

| (424.8) | (372.1) | (0.99,1.00) | (424.8) | (372.1) | 1.00 |
|---------|-----------|-------------|---------|-----------|-----|

Table 6.

Factors associated with high GV during non-haemodialysis day using simple logistic regression.
|                          | SD Target | SD High | Test statistic | P Value | Crude Odds ratio (95% CI) Target | SD | High | Test statistic | P Value | Crude Odds ratio (95% CI) Target | SD | High |
|--------------------------|-----------|---------|----------------|---------|----------------------------------|----|------|----------------|---------|----------------------------------|----|------|
| **Diabetes**             |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| No                       | 57 (41.9) | 0 (0)   | 1.866          | 0.06*   | 15.2 (0.88, 264.5)               |    |      |                |         |                                  |    |      |
| Yes                      | 79 (58.1) | 10      | Reference      | 57 (41.0) | 7 (100)                          |    |      |                |         |                                  |    |      |
| **Gender**               |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| Male                     | 76 (59.9) | 5       | 0.361          | 0.72    |                                  |    |      |                |         |                                  |    |      |
| Female                   | 60 (44.1) | 5       | Reference      | 77 (55.4) | 4                               |    |      |                |         |                                  |    |      |
| **Smoking**              |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| No                       | 122 (89.7)| 10      | 0.516          | 0.61    | 0.50 (0.02, 8.50)                |    |      |                |         |                                  |    |      |
| Yes                      | 12 (0.0)  | 0       | Reference      | 125 (89.9) | 0 (0)                          |    |      |                |         |                                  |    |      |
| **BMI**                  |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| Normal                   | 5 (18.5)  | 0 (0)   | 0.009          | 0.992   | 1.1 (0.05, 26.80)               |    |      |                |         |                                  |    |      |
| Underweight              | 24 (17.7) | 2       | 0.071          | 0.94    |                                  |    |      |                |         |                                  |    |      |
| (<18.5)                  | 21 (15.4) | 1       | 0.16           | 0.88    | 0.77 (0.03, 21.50)              |    |      |                |         |                                  |    |      |
| Overweight               | 54 (23.0) | 3       | 0.27           | 0.78    | 0.71 (0.03, 25.50)              |    |      |                |         |                                  |    |      |
| Obese 1                   | 32 (39.7) | 4       | 1.53           | 0.07    | 0.55 (13.6)                    |    |      |                |         |                                  |    |      |
| Obese 2 (18%)            | 32 (23.5) | 4       | 1.50           | 0.07    | 0.55 (13.6)                    |    |      |                |         |                                  |    |      |
| **IHD**                  |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| No                       | 99 (72.8)| 10      | 1.417          | 0.16    | 0.13 (0.01, 2.20)               |    |      |                |         |                                  |    |      |
| Yes                      | 37 (72.7)| 0       | Reference      | 102 (73.4) | 7 (100)             |    |      |                |         |                                  |    |      |
| **Gout**                 |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| No                       | 123 (90.4)| 10      | 0.563          | 0.57    | 0.44 (0.02, 7.80)               |    |      |                |         |                                  |    |      |
| Yes                      | 13 (9.6)  | 0       | Reference      | 126 (90.6) | 0 (0)               |    |      |                |         |                                  |    |      |
| **Hyperlipidaemia**      |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| No                       | 61 (44.9)| 2       | 1.458          | 0.15*   | 3.25 (0.78, 22.10)             |    |      |                |         |                                  |    |      |
| Yes                      | 75 (55.1)| 8 (80) | Reference      | 62 (44.6) | 1                               |    |      |                |         |                                  |    |      |
| **Stroke**               |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| No                       | 129 (94.9)| 10      | 0.131          | 0.90    | 0.82 (0.04, 15.40)             |    |      |                |         |                                  |    |      |
| Yes                      | 7 (5.1)  | 0       | Reference      | 132 (95.0) | 7 (100)             |    |      |                |         |                                  |    |      |
| **Hypertension**         |           |         |                |         |                                  |    |      |                |         |                                  |    |      |
| No                       | 4 (2.9)  | 0       | 0.222          | 0.82    | 0.71 (0.04, 14.20)             |    |      |                |         |                                  |    |      |
| Yes                      | 132 (97.1)| 10      | Reference      | 4 (2.9)  | 0 (0)                           |    |      |                |         |                                  |    |      |
| **Mean (SD)**            | 53.1 (11.8)| 58.4 (11.8)| 2.135         | 0.03*   | 1.07 (1.00, 1.40)             |    |      |                |         |                                  |    |      |
| **Mean (SD)**            | 4.1 (3.2) | 4.0 (3.2)| 0.428         | 0.67    | 1.04 (0.84, 1.26)             |    |      |                |         |                                  |    |      |
| **BMI (kg/m²)**          | 26.7 (5.4)| 27.1 (5.2)| 0.50          | 0.62    | 1.03 (0.91, 1.16)             |    |      |                |         |                                  |    |      |
| **HbA1c**                | 6.4 (1.6) | 7.4 (1.6)| 2.32          | 0.02*   | 1.49 (1.06, 2.10)             |    |      |                |         |                                  |    |      |
| **Ferritin**             | 7.3 (7.0)| 9.0 (9.8)| -0.689        | 0.49    | 0.96 (0.85, 1.05)             |    |      |                |         |                                  |    |      |
| **Mean (SD)**            | 632.9 (7.0)| 498.6 (9.8)| -1.165        | 0.25    | 0.99 (0.99, 1.05)             |    |      |                |         |                                  |    |      |
Table 6 shows simple logistic regression analysis of sociodemographic, clinical comorbidities and blood parameters among patients in cohort (n=150) with poor GV during NHD.

*Factors that were significant at p<0.15 to be included in multiple logistic regression.

Table 7.
Multivariate analysis for factors associated with high GV during haemodialysis day (n=148)

| SD Variables | β      | SE   | Wald | Adjusted OR (95% CI) | P-Value |
|--------------|--------|------|------|----------------------|---------|
| Diabetes     | 0.65   | 0.65 | 0.99 | 1.9 (0.5, 7.4)       | 0.32    |
| Age          | 0.027  | 0.02 | 1.27 | 1.0 (0.9, 1.1)       | 0.20    |
| HBA1C        | 0.26   | 0.16 | 1.60 | 1.3 (0.9, 1.8)       | 0.11    |
| Ferritin     | -0.007 | 0.0006 | -1.06 | 0.9 (0.9, 1.00) | 0.29    |
| LDL          | -0.479 | 0.234 | -2.05 | 0.6 (0.4, 0.9) | 0.04*   |
| TG           | 0.248  | 0.157 | 1.58 | 1.3 (0.9, 1.7)       | 0.11    |

| %CV Variables | β      | SE   | Wald | Adjusted OR (95% CI) | P-Value |
|---------------|--------|------|------|----------------------|---------|
| Diabetes      | 1.13   | 0.76 | 1.48 | 3.1 (0.7, 16.2)      | 0.14    |
| Age           | 0.05   | 0.02 | 2.0  | 1.0 (1.0, 1.1)       | 0.05*   |
| HBA1C         | 0.03   | 0.17 | 0.19 | 1.0 (0.7, 1.4)       | 0.85    |
| Ferritin      | -0.001 | 0.0008 | -1.54 | 0.9 (0.9, 1.0) | 0.12    |
| LDL           | -0.33  | 0.24 | -1.35 | 0.7 (0.4, 1.1) | 0.18    |

Table 7 shows multiple logistic regression analysis of significant factors associated with poor SD GV among ESKD patients during haemodialysis (HD) day. OR, odd ratio; R²= 0.22 (Nagelkerke) *p <0.05.
Table 8.
Multivariate analysis for factors associated with high GV during non-haemodialysis day (n=148)

| SD Variable | β    | SE   | Wald | Adjusted OR (95% CI) | P-Value |
|-------------|------|------|------|----------------------|---------|
| Diabetes    | 18.23| 2128.0| 0.01 | 83.3 (0.001, Inf)    | 0.99    |
| Age         | 0.54 | 0.97 | 0.56 | 1.7 (0.3, 1.5)       | 0.58    |
| HBA1C       | 0.03 | 0.04 | 0.75 | 1.0 (0.9, 1.1)       | 0.46    |
| Ferritin    | 0.22 | 0.25 | 0.88 | 1.2 (0.8, 2.1)       | 0.38    |
| Albumin     | 0.26 | 0.15 | 1.76 | 1.3 (1.0, 1.8)       | 0.08*   |

| %CV Variable | β    | SE   | Wald | Adjusted OR (95% CI) | P-Value |
|--------------|------|------|------|----------------------|---------|
| Diabetes     | 16.87| 2224.6| 0.008| 21.1 (0.03, Inf)     | 0.99    |
| Hyperlipidaemia | 0.92 | 1.2  | 0.77 | 2.5 (0.3, 5.4)       | 0.44    |
| Age          | 0.04 | 0.05 | 0.75 | 1.0 (0.9, 1.1)       | 0.45    |
| HBA1C        | 0.43 | 0.27 | 1.59 | 1.5 (0.9, 2.7)       | 0.11    |
| Albumin      | 0.21 | 0.15 | 1.39 | 1.2 (0.9, 1.7)       | 0.17    |

Table 8 shows multiple logistic regression analysis of significant factors associated with poor %CV GV among ESKD patients during non-haemodialysis day. OR, odds ratio; $R^2 = 0.31$ (Nagelkerke) *p < 0.05.

Table 9
Glycemic variability indices comparing haemodialysis and non-haemodialysis day based on medications (diabetes patients) (n =91)

| Medication   | Target (SD GV HDD) | High (SD HDD) | c statistic | P value |
|--------------|--------------------|---------------|-------------|---------|
| Insulin      | 33 (63.5)          | 19 (36.5)     | 1.1599      | 0.5599  |
| OHA          | 12 (75.0)          | 4 (25.0)      |             |         |
| No medication| 16 (69.5)          | 7 (30.5)      |             |         |

| Medication   | Target (%CV HDD) | High (%CV HDD) | c statistic | P value |
|--------------|------------------|----------------|-------------|---------|
| Insulin      | 40 (76.9)        | 12 (23.1)      | 0.25402     | 0.8807  |
| OHA          | 12 (75.0)        | 4 (25.0)       |             |         |
| No medication| 16 (69.5)        | 7 (30.5)       |             |         |
### Table 9

| Medication         | SD  | %CV NHDD | c statistic | P value |
|-------------------|-----|----------|-------------|---------|
| Insulin           | 44 (86.3) | 7 (13.7) | 0.81724     | 0.6646  |
| OHA               | 15 (93.8) | 1 (6.2)  |             |         |
| No medication     | 20 (86.9) | 3 (13.1) |             |         |

| Medication         | <36% (Target) | >36% (High) | c statistic | P value |
|-------------------|---------------|-------------|-------------|---------|
| Insulin           | 44 (86.3)     | 7 (13.7)    | 5.6609      | 0.05899 |
| OHA               | 16 (100)      | 0 (0)       |             |         |
| No medication     | 23 (100)      | 0 (0)       |             |         |

Table 9 shows the association between type of medications prescribed to patients in relation to glycemic variability indices; SD, standard deviation; %CV, percentage co-efficient variant; HDD, haemodialysis day; NHDD, non-haemodialysis day, OHA, oral-hypoglycemic agents.

### Table 10: Glycaemic pattern and variability comparing haemodialysis and non-haemodialysis day

Table 10 Glycaemic pattern and variability comparing haemodialysis and non-haemodialysis day (DM-ESKD: diabetic end-stage renal disease, NDM-ESKD: non-diabetic end-stage renal disease, GV: glycaemic variability, SMBG: self-monitor blood glucose, CGM: continuous glucose monitoring, SD: standard deviation, %CV: percentage co-efficient variant, MAGE: mean amplitude glucose excursion)
| Study                        | Population and methods                                                                 | Glycaemic profile pattern and GV                                      | Conclusion                                                                 |
|------------------------------|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------|
| Abe et al. (2007)[20]        | • n = 16 patients (DM-ESKD)                                                              | • Glycaemic profile and variability                                   | • Plasma glucose decrease by haemodialysis.                                |
|                              | • Mean HbA1c: 8.1 ± 1.2% (Poor control) vs. 5.8 ± 0.62% (good control)                   | • Plasma blood glucose decreases significantly between poor and good control during initial haemodialysis period as compared to 2hr and 4hr in haemodialysis. | • Hyperglycaemic observed post haemodialysis.                               |
|                              | • Method: Plasma blood glucose                                                           | • Poor control group: Hyperglycaemia appeared post haemodialysis due to decrease in insulin. | • Fluctuations more pronounced during haemodialysis vs non-haemodialysis day (poor control) |
| Kazempour-Ardenilli et al. (2009) [22] | • n = 17 patients (DM-ESKD)                                                              | • Glycaemic profile and variability                                   | • Glucose values are significantly lower on HD as compared to non-haemodialysis day. |
|                              | • Mean HbA1c: 6.9 ± 1.2%                                                                | • Mean (SD) blood glucose: 9.8 ± 3.8 mmol/L vs. 12.6 ± 5.6 mmol/L       | • Haemodialysis day had increase GV as compared to non-haemodialysis day.  |
|                              | • Method: CGM                                                                            | • 24hr AUC: 4694 ± 1988 mmol.3min⁻¹ vs. 5932.1 ± 2673.6 mmol.3min⁻¹     |                                                                           |
|                              | • GV indices: Mean, SD, AUC                                                              | • Hypoglycaemia: 3 (17%) had asymptomatic hypoglycaemia during first 24hrs |                                                                           |
| Mirani et al. (2010) [23]    | • n = 12 patients (DM-ESKD)                                                              | • Glycaemic profile and variability                                   | • Haemodialysis day had increase GV as compared to non-haemodialysis day.  |
|                              | • Mean HbA1c: 7.4 ± 1.1%                                                                | • Mean (SD) blood glucose: 10.32 ± 2.7 mmol/L vs. 8.5 ± 1.4 mmol/L       |                                                                           |
|                              | • Method: CGM                                                                            | • SD: 3.16 ± 1.7 mmol/L vs. 1.9 ± 0.6 mmol/L                           |                                                                           |
|                              | • GV indices: Mean, SD and MAGE                                                         | • MAGE: 4.16 ± 1.2 mmol/L vs. 3.18 ± 0.6 mmol/L                       |                                                                           |
|                              |                                                                                         | • Hypoglycaemia: 2 (11%) had asymptomatic occurring 6 hrs post dialysis |                                                                           |
| Jung et al. (2010)[24]       | • n = 9 patients (DM-ESKD)                                                               | • Glycaemic profile and variability                                   | • GV not affected by haemodialysis day.                                    |
|                              | • Mean HbA1c: 8.6 ± 1.2%                                                                | • No difference MAGE between haemodialysis and non-haemodialysis day.  |                                                                           |
|                              | • Method: CGM                                                                            | • More pronounced hypoglycaemia on haemodialysis day.                  |                                                                           |
|                              | • GV indices: Mean, SD, AUC and MAGE                                                     |                                                                        |                                                                           |

**Figures**
Gai et al. (2014) [25]  

- n = 12 patients (ESDN)  
- Mean HbA1c: 7.2 ± 1.0%  
- Method: CGM  
- GV indices: Mean, SD, MAGE  

Glycaemic profile and variability  

- All patients showed a decrease in blood glucose during starting haemodialysis with nadir attained at around 200 minutes into haemodialysis.  
- Post dialysis hyperglycaemia observed after 150 minutes.  
- Hypoglycaemia: 2 (16%) experienced asymptomatic hypoglycaemia  
- Mean blood glucose HD vs NHD: 7.88 mmol/L vs 7.27 mmol/L  

- Haemodialysis associated with a significant intra-dialytic reduction of glycaemia and post-dialytic hyperglycaemia.

Jin et al. (2015) [13]  

- n = 46 patients (DM-ESKD and NDM-ESKD)  
- Mean HbA1c: 7.3 ± 1.9%  
- Method: CGM  
- GV indices: Mean, SD and MAGE  

DM-ESKD group (haemodialysis vs. non-haemodialysis day)  

- Mean blood glucose: 11.05 ± 3.0 mmol/L vs. 12.33 ± 4.09 mmol/L  
- SD: 2.97 ± 1.12 mmol/L vs. 2.31 ± 1.24 mmol/L  
- MAGE: 7.54 ± 2.83 mmol/L vs. 5.24 ± 2.64

NDM-ESKD group (haemodialysis vs. non-haemodialysis day)  

- Mean blood glucose: 7.34 ± 2.3 mmol/L vs. 7.58 ± 2.14 mmol/L  
- SD: 1.39 ± 0.48 mmol/L vs. 0.95 ± 0.71 mmol/L  
- MAGE: 4.10 ± 2.02 mmol/L vs. 2.84 ± 2.89  

DM-ESKD had larger glycaemic fluctuations as compared to NDM-ESKD.  

GV more pronounced on haemodialysis vs. non-haemodialysis day.

**Figure 1**

Glycaemic pattern during haemodialysis day (HD) based on GV indices, i.e., SD and %CV. Both graphs show that glycaemic fluctuations were more marked among patients with high GV indices and in DM-ESKD. Timing: D1 = Fasting, D2 = Prior haemodialysis, D3 = 1st hour haemodialysis, D4 = 2nd hour haemodialysis, D5 = 3rd hour haemodialysis, D6 = 4th hour haemodialysis, D7 = 2 hours post haemodialysis, before meal, D8 = 2hrs post-meal, D9 = before dinner, D10 = 2 hours post-dinner, D11= before sleep.
Figure 2

Glycaemic pattern during non-haemodialysis day (N-HD) based on GV indices, i.e., SD and %CV. Both graphs show that glycaemic fluctuations were more marked among DM-ESD with high GV indices. No NDM-ESKD had high GV during non-haemodialysis day. Timing: ND1 = Fasting – before breakfast, ND2 = 2 hours post breakfast, ND3 = before lunch, ND4 = 2 hours post-lunch, ND5 = before dinner, ND6 = 2 hours post-dinner, ND7 = before sleep.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- questionnaireGV.pdf