

Hypoglycemia during Hemodialysis in patients with ESRD with or without having diabetes; An Observational Study

Abstract:

Background:

Patients with end-stage renal disease (ESRD) regardless of diabetes status are at increased risk of hypoglycemia due to dysregulation of the physiological processes maintaining normal glucose metabolism with a resultant array of adverse clinical outcomes endangering the life of patients.

Objective:

The aim of this study is to measure the occurrence of **hypoglycemia in patients of ESRD on hemodialysis with or without having diabetes** at specified intervals.

Methods:

This cross-sectional study will encompass 142 patients with ESRD on dialysis any age group with known ESRD, with or without having diabetes receiving dialysis for ≥ 3 months. It was done in dialysis wing, Department of Nephrology of MMCH. The study was occurred from February 2022 to July 2022. Sampling technique was purposive sampling.

Result:

Most of the patients (40.8%) were from 46-60 years of age group. In case of gender, male was predominant that was 69.7%. Regarding to diabetes mellitus, majority (80.3%) patients were free from this disease. On the other hand, 62.7% of patients were patient of hypertension. 130 patients had taken dialysis twice per week whereas, only 12 patients had taken dialysis thrice in a week. Most of patients had cardiovascular disease (51.7%) whereas only 10.3% patients were affected to diabetic foot. Moreover, most of the patients were found (45.5%) in level 2 hypoglycemia.

Conclusion:

Patients were more prone to have level 2 of hyperglycemia in both diabetic and non-diabetic patient. However, the diabetic patient had more chance of co-morbidities along with complications.

Introduction:

Patients with end-stage renal disease (ESRD), regardless of having diabetes mellitus are at increased risk of hypoglycemia with a resultant array of adverse clinical outcomes. Hypoglycemia occurs not infrequently in patients with ESRD, especially during hemodialysis sessions and is particularly common in those with diabetes mellitus ^[1]. (The reference should be Abe M, Kalantar-Zadeh K. Haemodialysis-induced hypoglycaemia and glycaemic disarrays. *Nat Rev Nephrol.* 2015 May;11(5):302-13. doi: 10.1038/nrneph.2015.38. Epub 2015 Apr 7. PMID: 25848881; PMCID: PMC6015632, and Jackson MA, Holland MR, Nicholas J, Lodwick R, Forster D, Macdonald IA. Hemodialysis-induced hypoglycemia in diabetic patients. *Clin Nephrol.* 2000 Jul;54(1):30-4. PMID: 10939754.) Dysregulation of the physiological processes maintaining normal glucose metabolism contribute to the development of hypoglycemia in ESRD ^[2]. Improved insulin sensitivity following the institution of renal replacement therapy (RRT), increased insulin clearance and diminished gluconeogenesis in the kidney and liver all result in the reduced rate of glucose appearance in the blood, which, in turn, increases dependence on the exogenous sources of carbohydrates ^[3]. Malnutrition, weight loss and a high incidence of infections may further reduce appearance of glucose from exogenous and endogenous sources, thereby contributing to the development of hypoglycemia in ESRD. This condition can be aggravated by hemodialysis of a bath that does not contain glucose and by the presence of acetate in the bath. Acetate inhibits the release of an insulin-counter regulatory hormone ^[4]. Symptomatic hypoglycemia (HG) during hemodialysis (HD) has been reported in chronic kidney disease (CKD) patients since more than a decade ago ^[5] and it is common in diabetic (DM) individuals when dialysis is performed with a glucose-free dialysis solution ^[6].

Severe hypoglycemia may result in some grave outcome like acute mental status changes, seizures, coma even death. One study suggested a link between hypoglycemia and increased risk of stroke in patients with renal failure ^[7]. Cardiac arrhythmias are another potential clinical manifestation of hypoglycemia ^[8]. ESRD patients can be more vulnerable to the neurological and cardiovascular effects of hypoglycemia due to the high prevalence of cardiovascular disease, dementia and administration of analgesics.

Type 2 diabetes mellitus (T2DM) is one of the leading causes of chronic kidney disease (CKD) and end-stage renal disease (ESRD) in developed and developing countries ^[9]. Annually, each patient with type 1 diabetes is at risk of experiencing 1–3 episodes and every other person with type 2 diabetes may have at least one episode of severe hypoglycemia ^[8]. It should be noted that current evidence suggests avoiding strict glycemic controlling ESRD patients ^[10].

The etiology of hypoglycemia in non-diabetic ESRD patient can be grouped in conditions associated with decreased or undetectable insulin level, and those within appropriately high insulin concentration. Malnutrition, alcohol abuse, organ failure, infections, drugs and/or adrenal insufficiency are among the frequently encountered clinical states in which hypoglycemia is most likely to be associated with hypo-insulinemia ^[11].

This study will help us to find the measure of occurrence of hypoglycemia during dialysis and the risk factors associated with it both in diabetic and non-diabetic subjects.

Material & methods:

This observational study will encompass 142 patients with ESRD on dialysis any age group with known ESRD, with or without having diabetes receiving dialysis for ≥ 3 months. It was done in dialysis wing, Department of Nephrology of MMCH. The study was occurred from February 2022 to July 2022. Sampling technique was purposive sampling. In this study, Patients will be selected after matching inclusion and exclusion criteria. Following this, the aim and objectives, study procedure and utility of the study will be explained to all of them. Then written informed consent will be taken from all patients. Demographic, family history, medical history, anthropometrics, type of renal disease, diabetes status and other related information of each subject will be recorded in a data sheet.

We performed frequency analysis as a descriptive analysis to observe the socio-demographic variables as well as clinical characteristics of the study.

All continuous data were presented as mean \pm standard deviation (SD). After the data was collected, data were compiled and edited accordingly. Finally, to fulfill the research objectives, different descriptive analyses were conducted using Statistical Package for Social Sciences version 25.

Inclusion criteria:

ESRD patients of any age groups (male and female) with or without having diabetes and underwent hemodialysis at least three months earlier.

Exclusion criteria:

- a) Patient with Adrenal insufficiency, hepatic disorder, asthma, malignancy.
- b) Patient with acute critical illness.
- c) Patient with severe malnutrition.
- d) Patients who had undergone renal transplantation before beginning dialysis.

Hypoglycemia: Blood glucose level <3.9 mmol (70 mg/dl) (ADA 2022, Chapter 6, Table 1).
Classification of hypoglycemia ^[12]

| | |
|-----------------------------|--|
| Level 1 hypoglycemia | Glucose level <3.9 mmol (70 mg/dl) and ≥ 3 mmol/L (54 mg/dl) |
| Level 2 hypoglycemia | Glucose level <3 mmol (54 mg/dl) |
| Level 3 hypoglycemia | A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia |

List 1 : Classification of hypoglycemia

Result:**Table 1: Sociodemographic characteristics of respondents (n=142)**

Table 1 below demonstrates, the sociodemographic characteristics of respondents. It is evident that, most of the patients (40.8%) were from 46-60 years of age group. In case of gender, male was predominant that was 69.7%.

| Trait | Frequency (n) | Percentage (%) |
|--------------------------|----------------|----------------|
| Age group (years) | | |
| 15-30 | 20 | 14.08 |
| 31-45 | 45 | 31.7 |
| 46-60 | 58 | 40.8 |
| ≥61 | 19 | 13.4 |
| Mean age | 45.49 ± 13.682 | |
| Gender | | |
| Male | 99 | 69.7 |
| Female | 43 | 30.3 |

Table 2: Frequency (%) of comorbidities among respondents (n= 142)

Table 2 below shows the frequency (5) of comorbidities among respondents. Regarding to diabetes mellitus, majority (80.3%) patients were free from this disease. On the other hand, 62.7% of patients were patient of hypertension.

| |
|--------------------------|
| Diabetes Mellitus |
|--------------------------|

| | | |
|---------------------|------------|-------------|
| Absent | 114 | 80.3 |
| Present | 28 | 19.7 |
| Hypertension | | |
| Present | 89 | 62.7 |
| Absent | 53 | 37.3 |

Figure 1: Distribution of patients according to numbers of dialysis per week (n=142)

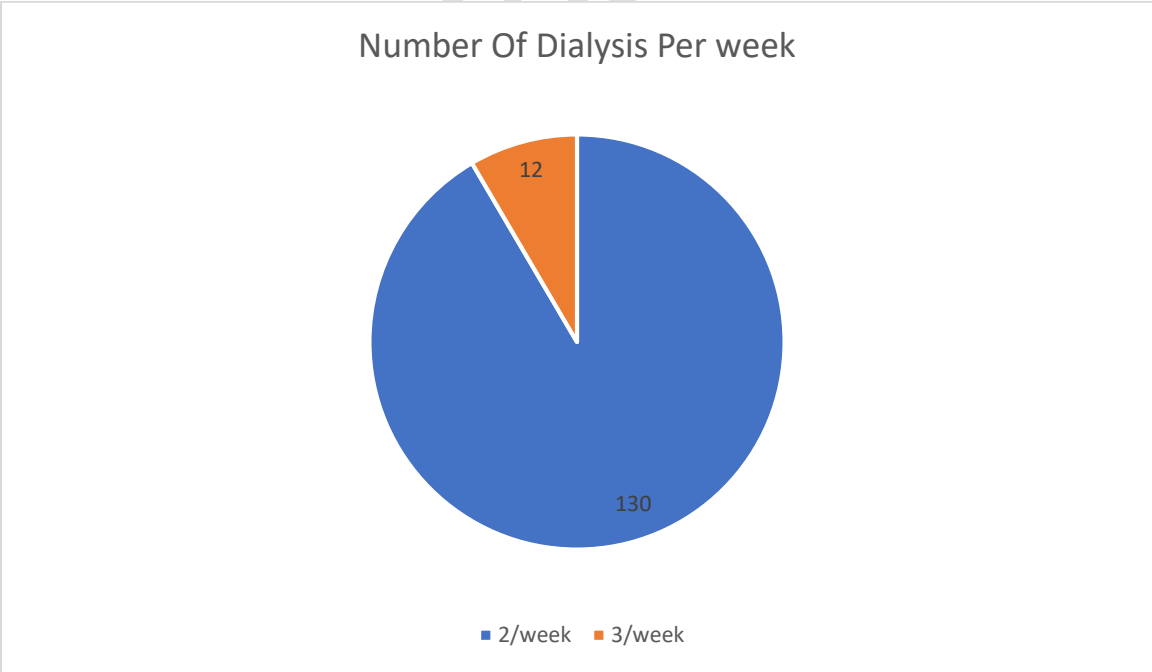


Figure 1 above illustrates, distribution of patients according to numbers of dialysis per week. It was found that, 130 patients had taken dialysis twice per week whereas, only 12 patients had taken dialysis thrice in a week.

Figure 2: Percentage (%) of the patients according to complications due to diabetes (n=29)

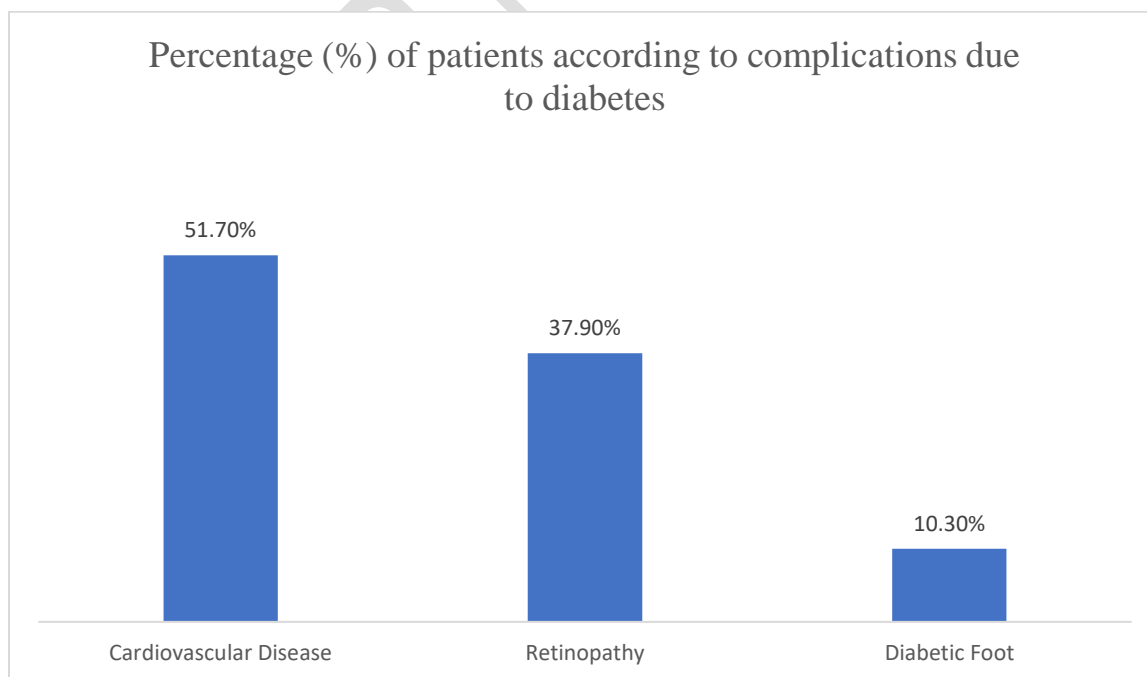


Figure 2 illustrates, the percentage (%) of patients according to complications due to diabetes. Most of patients had cardiovascular disease (51.7%) whereas only 10.3% patients were affected to diabetic foot.

Table 3: Distribution of hypoglycemia among the respondents (n=22)

Table 3 describes the distribution of hypoglycemia among respondents. It is evident that, most of the patients were found (45.5%) in level 2 hypoglycemia.

| Level of hypoglycemia | Frequency (n) | Percentage (%) |
|-----------------------|---------------|----------------|
| Level 1 | 5 | 22.7 |
| Level 2 | 10 | 45.5 |
| Level 3 (Severe) | 7 | 31.8 |

Discussion:

This cross-sectional study will encompass 142 patients with ESRD on dialysis any age group with known ESRD, with or without having diabetes receiving dialysis for ≥ 3 months. It was done in dialysis wing, Department of Nephrology of MMCH. The aim of this study is to measure the occurrence of hypoglycemia in patients of ESRD on hemodialysis with or without having diabetes at specified intervals.

In this study, the mean age of respondents was 45.49 ± 13.682 . In previous similar study, the mean age of population was 64.8 ± 5.4 [13].

In case of gender, male was predominant that was 69.7%. In previous study, men were more prone to do an arteriovenous fistula comparing to women (80% v/s 73%). However, there was no evidence of gender-specific differences in terms of dialysis adequacy [14].

Furthermore, according to this study, majority of the patients (51.7%) had cardiovascular disease. In a similar study, >60% of new dialysis patients complained of coronary atherosclerosis [15].

Moreover, according to the severity, out of 28 patient majority of them in this study (22.7% and 45.5%) were in level 1 (mild) and 2 (moderate) hypoglycemia. Similarly in previous study, almost half of the patients had (50.6%) one episode of hypoglycemia as only 10.7% patients experienced severe hypoglycemia [16].

Overall, hypoglycemia along with diabetes has more mortality and morbidities. In addition, Diabetic kidney disease is associated with cardiovascular disease.

When Dialysis is performed in glucose free solution, there is a huge tendency of hypoglycemia during dialysis specially in a diabetic patient. Glucose added dialysate can be a solution of preventing hypoglycemia in dialysis [17].

Conclusion:

Hypoglycemia can be also occurred in non-diabetic patients. There is a huge chance of having comorbidities along with complications in case of diabetic with patients. However, prospective studies with large size population are more suggested for clear conception.

Reference:

1. Akmal M. Hemodialysis in diabetic patients. *American Journal of Kidney Diseases*. 2001 Oct 1;38(4):S195-9.
2. Kovesdy CP, Park JC, Kalantar-Zadeh K. Glycemic control and burnt-out diabetes in ESRD. In *Seminars in dialysis* 2010 Mar (Vol. 23, No. 2, pp. 148-156). Oxford, UK: Blackwell Publishing Ltd.
3. Ferrannini E, Wahren JO, Faber OK, Felig PH, Binder CH, DeFronzo RA. Splanchnic and renal metabolism of insulin in human subjects: a dose-response study. *American journal of physiology-endocrinology and metabolism*. 1983 Jun 1;244(6):E517-27.
4. Orskov H, Hansen AP, Hansen HE, Alberti KG, Noy GA, Nosadini R. Acetate: inhibitor of growth hormone hypersecretion in diabetic and non-diabetic uraemic subjects. *Acta Endocrinologica*. 1982 Apr 1;99(4):551-8.
5. Jackson MA, Holland MR, Nicholas J, Talbot M, Spencer H, Lodwick R, Fuhrmann C, Forster D, Macdonald IA. Occult hypoglycemia caused by hemodialysis. *Clinical nephrology*. 1999 Apr 1;51(4):242-7.
6. Jackson, MA, Holland, MR, Nicholas, J, Lodwick, R, Foster, D, Macdonald, IA 2000, 'Hemodialysis-induced hypoglycemia in diabetic patients', *Clin Nephrol.*, vol. 54, pp. 30-4
7. Yu TM, Lin CL, Chang SN, Sung FC, Kao CH. Increased risk of stroke in patients with chronic kidney disease after recurrent hypoglycemia. *Neurology*. 2014 Aug 19;83(8):686-94.
8. Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L, Heller SR, Rodriguez H, Rosenzweig J, Vigersky R. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and the Endocrine Society. *The Journal of Clinical Endocrinology & Metabolism*. 2013 May 1;98(5):1845-59.

9. Collins AJ, Foley RN, Herzog C, Chavers BM, Gilbertson D, Ishani A, Kasiske BL, Liu J, Mau LW, McBean M, Murray A. Excerpts from the US renal data system 2009 annual data report. *American journal of kidney diseases*. 2010 Jan 1;55(1):A6-7.
10. Ricks J, Molnar MZ, Kovesdy CP, Shah A, Nissenson AR, Williams M, Kalantar-Zadeh K. Glycemic control and cardiovascular mortality in hemodialysis patients with diabetes: a 6-year cohort study. *Diabetes*. 2012 Mar 1;61(3):708-15.
11. Aidar FJ, de Oliveira RJ, de Matos DG, Mazini Filho ML, Moreira OC, de Oliveira CE, Hickner RC, Reis VM. A randomized trial investigating the influence of strength training on quality of life in ischemic stroke. *Topics in stroke rehabilitation*. 2016 Feb 17;23(2):84-9.
12. Field JB. Hypoglycemia: definition, clinical presentations, classification, and laboratory tests. *Endocrinology and metabolism clinics of North America*. 1989 Mar 1;18(1):27-43.
13. Haviv YS, Sharkia M, Safadi R. Hypoglycemia in patients with renal failure. *Renal failure*. 2000 Jan 1;22(2):219-23.
14. Weigert A, Drozd M, Silva F, Frazao J, Alsuwaida A, Krishnan M, Kleophas W, Brzosko S, Johansson FK, Jacobson SH. Influence of gender and age on haemodialysis practices: a European multicentre analysis. *Clinical Kidney Journal*. 2020 Apr;13(2):217-24.
15. Stack AG, Bloembergen WE. Prevalence and clinical correlates of coronary artery disease among new dialysis patients in the United States: a cross-sectional study. *Journal of the American Society of Nephrology*. 2001 Jul 1;12(7):1516-23.
16. Gianchandani RY, Neupane S, Heung M. Hypoglycemia in hospitalized hemodialysis patients with diabetes: an observational study. *Journal of Diabetes Science and Technology*. 2018 Jan;12(1):33-8.
17. Burmeister JE, Miltersteiner DD, Burmeister BO, Campos JF. Risk of hypoglycemia during hemodialysis in diabetic patients is related to lower pre-dialysis glycemia. *Archives of endocrinology and metabolism*. 2015;59:137-40.