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# EVALUATION OF CONTROL OF DIABETES MELLITUS IN HEMODIALYSIS PATIENTS: PERSPECTIVE STUDY

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## INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder resulting from a defect in insulin secretion and/or insulin action, which results in hyperglycemia with disturbances of carbohydrate, fat and protein metabolism ***(Hovens, et al.,2005).***

Diabetes mellitus is a major health problem of increasing magnitude worldwide with a great impact on cardiovascular morbidity and mortality ***(Grundy et al.,2002).***

Diabetes mellitus is recognized as a leading cause of chronic kidney disease and end-stage renal failure. Chronic renal failure is associated with insulin resistance and, in advanced renal failure, decreased insulin degradation. Both of these abnormalities are partially reversed with the institution of dialysis ***(Ch Samapanis,2008).***

Chronic kidney disease (CKD) is common and can be found in up to 23% of patients with diabetes. The recommended hemoglobin A1c goal for these patients is also < 7.0%. Medication therapy for diabetes may require dose adjustments or may be contraindicated in patients with CKD. Assessment and management of comorbid diseases, including hypertension, hyperlipidemia, anemia, hyperphosphatemia, and hyperparathyroidism, is important in the care of patients with diabetes and CKD. Multidisciplinary care may provide the optimal system for maximizing care of these complex patients (Kerri. Cavanaugh***, 2007).***

Management of diabetes includes many areas that may be influenced by the severity of a patient's kidney dysfunction. This includes the methods that are used to determine the adequacy of diabetes control, such as hemoglobin A1c (A1C), the potential complications and cautions regarding oral hyperglycemic therapies, and the variable response to insulin therapy as kidney dysfunction progresses. Additionally, management of comorbid conditions, such as hypertension and hyperlipidemia, and evaluation for the development of conditions associated with CKD, such as anemia, hyperphosphatemia, and hyperparathyroidism, must also be considered in the care of patients with diabetes and CKD (Kerri, Cavanaugh***,2007).***

For most hemodialysis patients, we use insulin rather than oral agents. This is consistent with the 2005 K/DOQI guidelines, which suggest that, among dialysis patients, newer insulin regimens and insulin preparations should be used rather than oral agents for glycemic control This is due to the lack of adequate data concerning the use of oral agents in dialysis patients and their inability to adequately excrete many such agents ***(K/DOQI Workgroup,2005).***

## AIM OF THE WORK

The aim of the study is to find out the prevalence of diabetes mellitus in hemodialysis patients and the possible medications for control of their blood glucose level taking into consideration their precautions , contraindications and side effects and the current diabetic complications already seen in hemodialysis patients.

## PATIENTS AND METHODS

### Patients and Methods.

The study was carried out on adult patients on Hemodialysis in all dialysis units in Minia governorate and we screen the number of diabetic patients on hemodialysis and their data about their blood glucose levels and the hypoglycemic drugs they are taking. A performed questioner was fulfilled for all study subjects. The El-Minia Governorate is one of Egypt's 28 Governorates and is located about 143 miles to the south of Cairo; it comprises nine districts (Edwa**,** Maghagha, Bany Mazar, Mattay, Samalout, El-Minia, Abou Korkas Malawy and Deir Mawas). Of the 1700 patients on RRT who were offered to participate in this study, 755 patients (44.4%) agreed and gave verbal consent.

### The questioner gave data about;

1) The number of diabetic patients in dialysis units in Minia governorate, precenrage of controlled diabetic patients on hemodialysis, blood glucose lowering drugs they were taking ,family history of diabetes mellitus (DM) and complications of DM.

2) Presence of HCV infection including total number of hemodialysis patients having HCV infection,the number of diabetic patients having HCV virus and probable causes of renal failure.

3)Body mass index for all hemodialysis patients , Random blood glucose level for all hemodialysis patients , Glycosylated Hb(HbA1c) for diabetic patients only.

The study was carried out in the period between Feb 2016 to Feb 2017.

Patients age was ranged between 15 years old and 95 years old, and there was 491 males and 264 females.

**Patients in our study were divided into 3 groups as follow:**
**Group (1):** Include non diabetic patients.
**Group (2):** Include patients with blood glucose controlled: Groups A,B,C,D) :

Group (A) Include diabetic patients with blood glucose controlled without any blood glucose lowering medications.

Group (B) Include diabetic patients with blood glucose controlled with insulin only.

Group (C) Include diabetic patients with blood glucose controlled with both insulin and oral hypoglycemic drugs.

Group (D) Include diabetic patients with blood glucose controlled with oral hypoglycemic drugs only.

**Group (3) :** Include patients with blood glucose uncontrolled : (Groups A,B,C,D)

Group (A) Include diabetic patients with blood glucose not controlled with insulin.

Group(B) Include diabetic patients with blood glucose not controlled with oral hypoglycemic drugs.

Group(C) Include diabetic patients with blood glucose not controlled with both oral hypoglycemic drugs and insulin.

Group(D) Include diabetic not controlled without any blood glucose lowering medications.

**Exclusion criteria:**
1) Patients with other factors that can interfere with good control of DM as Those who are taking medication that may cause rapid glucose rise e.g. steroids, antipsychotics.
2) Patients with history of intake antidiabetic drugs for less than 2 months.
3) Patients with acute pancreatic damage, including pancreatic surgery.

**METHODS :**
**For all the cases the following was done:**
**a) full history taking.**
**b) full clinical general examination.**
**c) Anthropometric measures:** body mass index **.**

**Body weight:**
Was measured using an electronic scale to the nearest 0.1 Kg,with the subjects wearing light clothes and no shoses.

**Height:**
Was measured to the nearest 0.5 cm without shoes.

**Body mass index(BMI):**
Was calculated as weight (in kilograms) divided by the square of hight(in meters).

**Interpretation of higher Obesity risk:**
The WHO regards a BMI of less than 18.5 as underweight and may indicate malnutrition, an eating disorder, or other health problems, while a BMI equal to or greater than 25 is considered overweight and above 30 is considered obese. ***(BMI Classification .WHO 2006)*** **.** These ranges of BMI values are valid only as statistical categories.

| CATEGORY | BMI (KG/M$^2$) | | BMI PRIME | |
|---|---|---|---|---|
| | from | to | from | to |
| Very severely underweight | | 15 | | 0.60 |
| Severely underweight | 15 | 16 | 0.60 | 0.64 |
| Underweight | 16 | 18.5 | 0.64 | 0.74 |
| Normal (healthy weight) | 18.5 | 25 | 0.74 | 1.0 |
| Overweight | 25 | 30 | 1.0 | 1.2 |
| Obese Class I (Moderately obese) | 30 | 35 | 1.2 | 1.4 |
| Obese Class II (Severely obese) | 35 | 40 | 1.4 | 1.6 |
| Obese Class III (Very severely obese) | 40 | | 1.6 | |

**d)laboratory investigations:**
**1) routine investigations**
**2)special investigations**
**The routine investigations includes the following:**
**Renal function tests:**
- Serum creatinine.
- Predialysis blood urea.
- Postdialysis blood urea.

**Complete blood picture (CBC) .**
**Urine analysis for proteinuria.**
**Random blood glucose:**
The following Table summarises the 2006 WHO recommendations for the diagnostic criteria for diabetes and intermediate hyperglycaemia.

**Diabetes**
Fasting plasma glucose ≥7.0mmol/l (126mg/dl)
2–h plasma glucose* **or** ≥11.1mmol/l (200mg/dl)
Random venous plasma glucose concentration ≥ 11.1 mmol/l

**Impaired Glucose Tolerance (IGT)**
Fasting plasma glucose <7.0mmol/l (126mg/dl)
2–h plasma glucose* **and** ≥7.8 and <11.1mmol/l (140mg/dl and 200mg/dl)

**Impaired Fasting Glucose (IFG)**
Fasting plasma glucose 6.1 to 6.9mmol/l
2–h plasma glucose* (110mg/dl to 125mg/dl) **and (if measured)** <7.8mmol/l (140mg/dl)

- Venous plasma glucose 2–h after ingestion of 75g oral glucose load
- If 2–h plasma glucose is not measured, status is uncertain as diabetes or IGT cannot be excluded

**HCV Ab. by using ELISA Technique.**
**HBsAg. By using ELISA Technique.**
**Fundus examination for retinopathy.Special Investigation:**
**HbA1c** for diabetic**.**

An HbA1c of 48mmol/mol (6.5%) is recommended as the cut off point for diagnosing diabetes. A value of less than 48mmol/mol (6.5%) does not exclude diabetes diagnosed using glucose tests.

**Sampling:**
1- 6 ml of blood was taken from each patient 4 ml predialysis and 2ml postdialysis under strict a septic technique and was left to clot for one hour , serum was taken **:**

Predialysis tube for predialysis blood urea , serum creatinine , HCV Ab and HBsAg.

Post dialysis tube for post dialysis urea.
Another 4ml of blood was taken for HbA1c and CBC .
Random blood glucose was measured by skin prick test.

**Technique for measuring HbA1c:**
**1) Prepare sample**
Add 5 ul whole blood to the test tube with R1/Reagent. Mix well.

Leave the tube for minimum 2 minutes, maximum 3 minutes .Use a timer.

**Note** Equilibrate the R1/ Reagent to room temperature (20-25 c) before use.

### 2) Apply sample

Remix to obtain a homogenous suspension. Apply 25 ul of the mixture to a TD/Test Device. Hold the pipette approx. 0.5 cm above the test well and empty the pipette quickly in the middle of the test well. Allow the mixture to soak completely into the membrane. Wait for minimum 10 seconds.

**Note** Avoid air bubbles.

### 3) Apply R2/Washing Solution

Apply 25 ul R2/Washing Solution to the TD/Test Device. Allow the reagent to soak completely into the membrane. Wait for minimum 10 seconds.

**Note** Avoid air bubbles.

### 4) READ THE TEST RESULT

Read the test result within 5 minutes using NycoCard READER 11 instruction manual.

## RESULTS

Out of the 1700 patients on regular hemodialysis (HD) in El Minia governorate ,only 755 patients (44.4%) agreed to participate in this study, their age range 15-95 years .the mean age of all patients in our study was 50.4±14.3 years.The results showed that the incidence of ESRD was more in male patients 62.3% (n=470) than female patients 37.7% (n=285) (table 1).

**Table (1): demographic and clinical characteristics of the studied patients**

| Variable | Total =755 | |
|---|---|---|
| **Age (years)**<br>**Range**<br>**Mean±sd** | 15-95<br>50.4±14.3 | |
| **Sex**<br>**Males**<br>**Females** | 470<br>285 | 62.3%<br>37.7% |
| **BMI**<br>**Range**<br>**Mean±sd** | 18-35<br>24.3±2.5 | |
| **Dialysis duration**<br>**Range**<br>**Mean±sd** | 1month-27 years<br>3.8±3.4years | |
| **HCV** | 376 | 49.8% |
| **Family history of DM** | 48 | 6.3% |

Random blood glucose (RBG) range between 75-300 mg/dl ,the mean RBG was117.6±28.9 .(Table 2).

**Table (2): laboratory data characteristics of the studied patients**

| Variable | Total =755 | |
|---|---|---|
| | **Range** | **Mean±sd** |
| **RBS** | 75-300 | 117.6±28.9 |
| **HB%** | 4.3-19.8 | 9.5±2.001 |
| **Serum creatinine** | 1.6-14.6 | 6.4±1.9 |
| **Urea pre** | 16-414 | 136.9±36.5 |
| **Urea post** | 20-105 | 56.9±14.1 |

In our study the overall prevalence of diabetes in hemodialysis patients were 116 out of 755 with percentage of 15.4% and 639 not diabetic (84.6%) with P 0.001* . there is male excess in diabetes , 67 males in number were affected with DM (57.8%) and 49 female in number were affected with DM (42.2%) and family history of diabetes was observed in 48 patients with percentage 6.3% (Table 3,fig 1).

**Table (3): DM among hemodialysis patients:**

| Variable | Total =755 | |
|---|---|---|
| | No | % |
| **DM among hemodialysis** | 116 | 15.4% |

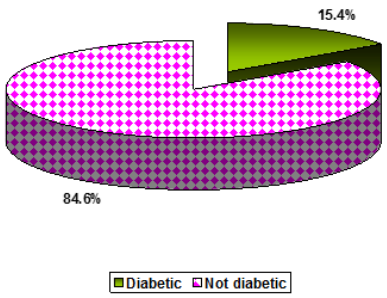


**Figure (1): DM among hem dialysis patients:**

Out of 116 ,there were 60 patients receiving insulin only (51.7%) , 30 patients receving oral hypoglycemic drugs (25.9%), 2 receving both oral hypoglycemic drugs and insulin (1.7%) and 24 patients not receiving any medications (20.7%) (Table 4).

**Table (4): treatment of DM among hemodialysis patients:**

| Variable | Total =116 | |
|---|---|---|
| | **No** | **%** |
| **Insulin only** | 60 | 51.7% |
| **Oral hypoglycemic** | 30 | 25.9% |
| **both** | 2 | 1.7% |
| **No medication** | 24 | 20.7% |

It was observed that retinopathy is the most common complications of DM in hemodialysis patients (26.7%) followed by nephropathy (17%) followed by hypoglycemia (11.2%). And the least complications of DM that observed in our study is diabetic ketoacidosis (3.4%) (Table 5,fig 2).

**Table (5): Diabetic complication**

| Variable | Total =116 | |
|---|---|---|
| | **No** | **%** |
| **No complication** | 34 | 29.3% |
| **Retinopathy** | 31 | 26.7% |
| **Hypoglycemia** | 13 | 11.2% |
| **Nephropathy** | 17 | 14.7% |
| **Cardiac** | 7 | 6% |
| **Neuropathy** | 10 | 8.6% |
| **DKA** | 4 | 3.4% |

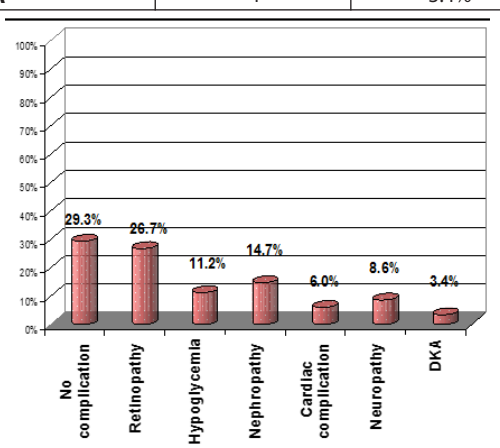


**Figure (2): Diabetic complication**

As regard causes of ESRD, we discovered that hypertension is the most common cause of renal failure (64.8%) followed by obstructive uropathy (16%) followed by diabetes mellitus ( 15.4%) (Table 6,fig 3).

**Table (6): Causes of chronic renal failure:**

| Variable | Total =755 | |
|---|---|---|
| | No | % |
| HTN | 489 | 64.8% |
| DM | 116 | 15.4% |
| OBSTRUCTED | 121 | 16% |
| INFLAMATORY | 61 | 8.1% |
| NSAID | 29 | 3.8% |
| OTHERS | 28 | 3.7% |
| DONOT KNOW | 60 | 7.9% |

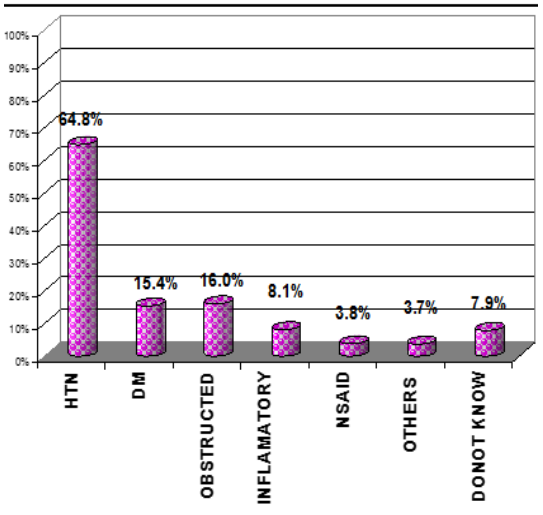


**Figure (3): Causes of chronic renal failure:**

In our study there was 63 hemodialysis patients with blood glucose controlled (by HbA1c) with percentage of 54.3% and 53 hemodialysis patients were uncontrolled with percentage of 45.7% (Table 7).

**Table (7): HA1-C of Diabetic patient**

| Variable | Total =116 | |
|---|---|---|
| | No | % |
| Controlled | 63 | 54.3% |
| Un controlled | 53 | 45.7% |
| Range | 2.1-15.7 | |
| Mean ±sd | 7.1±2.02 | |

Patients in our study were divided into 9 groups and results as follow: (Table 8).

**Table (8): Grouping of the studied patients**

| Groups | Groups | Total =755 | |
|---|---|---|---|
| | | No | % |
| Group (1): Include non diabetic patients | Not diabetic | 639 | 84.6% |
| Group 2 with blood glucose controlled | A. Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 1.9% |
| | B. Diabetic controlled with insulin only. | 32 | 4.2% |
| | C. Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 0.3% |
| | D. Diabetic controlled with oral hypo glycemic drugs only. | 15 | 2% |
| Group 3 Include patients with blood glucose uncontrolled | A. Diabetic not controlled with insulin. | 28 | 3.7% |
| | B. Diabetic not controlled with oral hypoglycemic drugs. | 15 | 2% |
| | C. Diabetic not controlled with both oral hypoglycemic drugs and insulin. | 0 | 0% |
| | D. Diabetic not controlled without any blood glucose lowering medications. | 10 | 1.3% |

Table 9 shows significant difference in age of studied patients (p-value=0.001*).

**Table (9): age distribution of the studied groups**

| Groups | Groups | Total | AGE (Mean ±sd) | P |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 49.1±14.4 | 0.001* |
| Group 2 with blood glucose controlled | A. Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 59±12.2 | |
| | B. Diabetic controlled with insulin only. | 32 | 57.3±13.8 | |
| | C. Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 58±5.6 | |
| | D. Diabetic controlled with oral hypoglycemic drugs only. | 15 | 57.06±9.8 | |
| Group 3 Include patients with blood glucose uncontrolled | A. Diabetic not controlled with insulin. | 28 | 56.7±10.9 | |
| | B. Diabetic not controlled with oral hypoglycemic drugs. | 15 | 58.8±8.5 | |
| | C. Diabetic not controlled without any blood glucose lowering medications. | 10 | 59.5±8.9 | |
| | D. Diabetic not controlled without any blood glucose lowering medications. | 10 | 59.5±8.9 | |

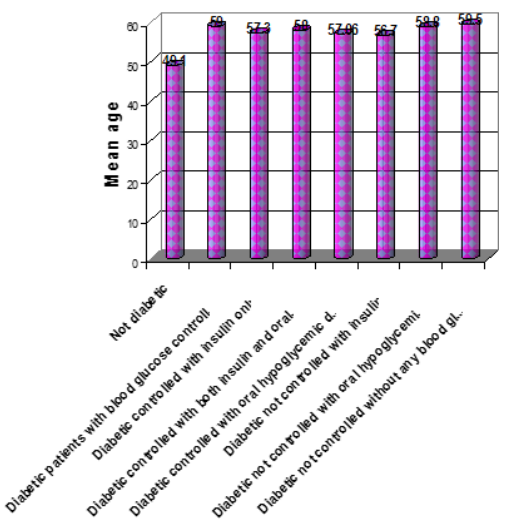


**Fig 4 Shows age distribution of the studied groups**

**Table (10): Sex distribution of the studied groups**

| Groups | Groups | Total | Male | Female | P |
|---|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 403(63.1%) | 236 (36.9%) | 0.3 |
| Group 2 with blood glucose controlled | A. Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 9(64.3%) | 5(35.7%) | |
| | B. Diabetic controlled with insulin only. | 32 | 22(68.8%) | 10(31.3%) | |
| | C. Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 1(50%) | 1(50%) | |
| | D. Diabetic controlled with oral hypoglycemic drugs only. | 15 | 5(33.3%) | 10(66.7%) | |
| Group 3 Include patients with blood glucose uncontrolled | A. Diabetic not controlled with insulin. | 28 | 16(57.1%) | 12(42.9%) | |
| | B. Diabetic not controlled with oral hypoglycemic drugs. | 15 | 7(46.7%) | 8(53.3%) | |
| | C. Diabetic not controlled without any blood glucose lowering medications. | 10 | 7(70%) | 3(30%) | |

Table 11 shows significant difference in BMI of studied patients (p-value =0.001*).

**Table (11): BMI of the studied groups**

| | Groups | Total | BMI (Mean ±sd) | P |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 24.1±2.4 | 0.001 |
| Group 2 with blood glucose controlled | A.Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 25±2.5 | |
| | B.Diabetic controlled with insulin only. | 32 | 26.2±3.4 | |
| | C.Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 26.5±0.7 | |
| | D.Diabetic controlled with oral hypoglycemic drugs only. | 15 | 25.1±2.3 | |
| Group 3 Include patients with blood glucose uncontrolled | A.Diabetic not controlled with insulin. | 28 | 25±2.5 | |
| | B.Diabetic not controlled with oral hypoglycemic drugs. | 15 | 26.4±2.7 | |
| | C.Diabetic not controlled without any blood glucose lowering medications. | 10 | 25.9±2.3 | |

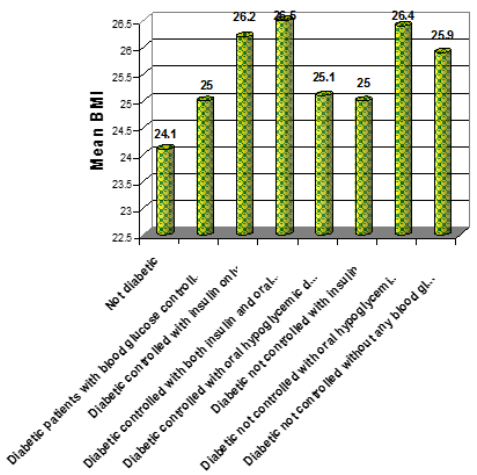


**Fig 5: Shows BMI of the studied groups.**

HCV was in 376 patients out of total 755 by percentage 49.8% (Table 12).

**Table (12): HCV among the studied groups**

| | Groups | Total | Positive HCV | Negative HCV |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 325(50.9%) | 314 (49.1%) |
| Group 2 with blood glucose controlled | A.Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 6(42.9%) | 8(57.1%) |
| | B.Diabetic controlled with insulin only. | 32 | 14(43.8%) | 18(56.2%) |
| | C. controlled with both insulin and oral hypoglycemic drugs. | 2 | 2(100%) | 0 |
| | D.Diabetic controlled with oral hypoglycemic drugs only. | 15 | 8(53.3%) | 7(46.7%) |
| Group 3 Include patients with blood glucose uncontrolled | A.Diabetic not controlled with insulin. | 28 | 10(35.8%) | 18(64.3%) |
| | B.Diabetic not controlled with oral hypoglycemic drugs. | 15 | 8(53.3%) | 7(46.7%) |
| | C.Diabetic not controlled without any blood glucose lowering medications. | 10 | 3(10%) | 7(70%) |

**Table (13): HB of the studied groups**

| | Groups | Total | HB (Mean ±sd) | P |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 9.5±2.4 | 0.5 |
| Group 2 with blood glucose controlled | A.Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 9.8±0.7 | |
| | B.Diabetic controlled with insulin only. | 32 | 9.8±1.9 | |
| | C.Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 10.8±0.1 | |
| | D.Diabetic controlled with oral hypoglycemic drugs only. | 15 | 8.8±1.9 | |
| Group 3 Include patients with blood glucose uncontrolled | A.Diabetic not controlled with insulin. | 28 | 10.1±1.6 | |
| | B.Diabetic not controlled with oral hypoglycemic drugs. | 15 | 9.5±1.9 | |
| | C.Diabetic not controlled without any blood glucose lowering medications. | 10 | 9.4±1.8 | |

Table 14 :shows significant difference in RBS in diabetic and non diabetic patients (p=0.001*).

**Table (14): RBS of the studied groups**

| | Groups | Total | RBS (Mean ±sd) | P |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 111.9±13.8 | 0.001* |
| Group 2 with blood glucose controlled | A.Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 125.2±35.06 | |
| | B.Diabetic controlled with insulin only. | 32 | 129.3±47.7 | |
| | C.Diabetic controlled with bot h insulin and oral hypoglycemic drugs. | 2 | 137±22.6 | |
| | D.Diabetic controlled with oral hypoglycemic drugs only. | 15 | 118±26.6 | |
| Group 3 Include patients with blood glucose uncontrolled | A.Diabetic not controlled with insulin. | 28 | 180.2±56.6 | |
| | B.Diabetic not controlled with oral hypoglycemic drugs. | 15 | 158.1±48.6 | |
| | C.Diabetic not controlled without any blood glucose lowering medications. | 10 | 194.1±37.4 | |

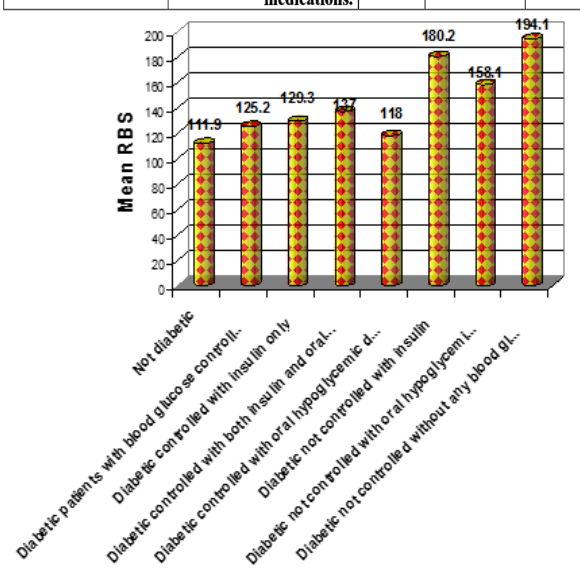

**Table (15): Urea pre treatment of the studied groups**

| | Groups | Total | Urea pre (Mean ±sd) | P |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 137.3±36.4 | 0.4 |
| Group 2 with blood glucose controlled | A.Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 142.5±15.01 | |
| | B.Diabetic controlled with insulin only. | 32 | 132.2±20.6 | |
| | C.Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 158±25.4 | |
| | D.Diabetic controlled with oral hypoglycemic drugs only. | 15 | 121.4±31.7 | |
| Group 3 Include patients with blood glucose uncontrolled | A.Diabetic not controlled with insulin. | 28 | 136.5±27.2 | |
| | B.Diabetic not controlled with oral hypoglycemic drugs. | 15 | 148±82.4 | |
| | C.Diabetic not controlled without any blood glucose lowering medications. | 10 | 125.8±20.4 | |

**Table (16): Urea post treatment of the studied groups**

| | Groups | Total | Urea post (Mean ±sd) | P |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 57.4±14.3 | 0.1 |
| Group 2 with blood glucose controlled | A.Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 55.7±9.6 | |
| | B.Diabetic controlled with insulin only. | 32 | 55.2±12.7 | |
| | C.Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 78.5±30.4 | |
| | D.Diabetic controlled with oral hypoglycemic drugs only. | 15 | 52.2±14.2 | |
| Group 3 Include patients with blood glucose uncontrolled | A.Diabetic not controlled with insulin. | 28 | 51.4±8.9 | |
| | B.Diabetic not controlled with oral hypoglycemic drugs. | 15 | 56.2±15.6 | |
| | C.Diabetic not controlled without any blood glucose lowering medications. | 10 | 55.3±9.7 | |

**Table (17): Serum creatinin of the studied groups**

| | Groups | Total | Urea post (Mean ±sd) | P |
|---|---|---|---|---|
| Group (1): Include non diabetic patients. | Not diabetic | 639 | 6.5±2.02 | 0.3 |
| Group 2 with blood glucose controlled | A.Diabetic patients with blood glucose controlled without any blood glucose lowering medications. | 14 | 5.7±0.6 | |
| | B.Diabetic controlled with insulin only. | 32 | 6.009±1.03 | |
| | C.Diabetic controlled with both insulin and oral hypoglycemic drugs. | 2 | 6±0.9 | |
| | D.Diabetic controlled with oral hypoglycemic drugs only. | 15 | 6.4±1.7 | |
| Group 3 Include patients with blood glucose uncontrolled | A.Diabetic n ot controlled with insulin. | 28 | 6.1±1.9 | |
| | B.Diabetic not controlled with oral hypoglycemic drugs. | 15 | 5.8±1.1 | |
| | C.Diabetic not controlled without any blood glucose lowering medications. | 10 | 6.2±1.8 | |

## DISCUSSION

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period ***(WHO, "About diabetes,2014)*.**

As of 2016, 422 million people have diabetes worldwide, ***(World Health Organization,2016)*** . up from an estimated 382 million people in 2013 ***(Shi,et al ;2014)*** .and from 108 million in 1980 (World Health Organization,2016). Accounting for the shifting age structure of the global population, the prevalence of diabetes is 8.5% among adults, nearly double the rate of 4.7% in 1980 ***(World Health Organization,2016)***. Type 2 makes up about 90% of the cases ***(Williams textbook of endocrinology ,12th ed., Vos T, et al 2012).*** Some data indicate rates are roughly equal in women and men, ***(Vos et al.,2012).*** but male excess in diabetes has been found in many populations with higher type 2 incidence, possibly due to sex-related differences in insulin sensitivity, consequences of obesity and regional body fat deposition, and other contributing factors such as high blood pressure, tobacco smoking, and alcohol intake ***(Gale et al., 2001, Meisinger et al.,2002).***

The World Health Organization (WHO) estimates that diabetes mellitus resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death (World Health Organization 2013., World Health Organization,2016). However another 2.2 million deaths worldwide were attributable to high blood glucose and the increased risks of cardiovascular disease and other associated complications (e.g. kidney failure), which often lead to premature death and are often listed as the underlying cause on death certificates rather than diabetes ***(World Health Organization, 2016, Public Health Agency of Canada, 2011).***

Diabetic nephropathy is the leading cause of end-stage renal failure (ESRF) ***(Coresh et al.,2007),*** representing 30–45% of the U.K. and U.S. (USRDS 2007) populations undergoing long-term maintenance hemodialysis. Hypoglycemia is common because of impaired renal gluconeogenesis, malnutrition, and the increased half-life of insulin and hypoglycemic agents ***(KDOQI,2007).*** The annual mortality among diabetic patients undergoing hemodialysis is high and is predominately due to cardiovascular disease (CVD) ***(USRDS,2007).*** Diabetic nephropathy is the leading cause of chronic kidney disease in patients starting renal replacement therapy ***(US Renal Data System: USRDS 2003)*** and is associated with increased cardiovascular mortality ***(Valmadrid et al.,2000).***

A history of diabetes, hypertension, or cardiovascular disease (CVD) confers the highest risk for developing CKD, and individuals who have such a history should be screened (Levey ***et al.,2007).***

Intensive glycemic management delays progression of microvascular disease ***(American Diabetes Association. 2002; Diabetes Control and Complications Trial2005; Action to Control Cardiovascular Risk in Diabetes Study Group.2008; ADVANCE Collaborative Group.2008)*** and improves malnutrition ***(Cano et al.,2002);*** however, large randomized controlled trials show no mortality benefit in high-risk groups with CVD ***(Action to Control Cardiovascular Risk in Diabetes Study Group. 2008); American Diabetes Association. 2008).*** Hypoglycemic events increase with intensive treatment and in the presence of CVD can cause fatal dysrhythmia ***(Diabetes Control and Complications Trial Research Group.1993).*** U.K. diabetes guidelines advise against intensive treatment aimed to lower A1C levels <6.5% ***(NICE, 2008),*** whereas American guidelines caution against values <7% ***(American Diabetes Association ,2007).*** No evidence-based guidelines for the glycemic targets for diabetic patients with ESRF undergoing long-term maintenance hemodialysis are available.

Optimum glycaemic control of diabetic patients with CKD is a topic of considerable uncertainty and confusion ***(Slinin et al.,2012).*** In diabetic patients with ESRD receiving chronic haemodialysis, several large observational studies have highlighted the risks associated with low haemoglobin A1c (HbA1c) levels. Data from these studies suggest that not only hyperglycaemia, but also low glucose levels (<5.55 mmol/l) are associated with increased mortality risk ***(Williams et al.,2006& Kalantar-Zadeh et al.,2007& Ricks et al.,2012).***

Although benefits associated with better glycemic control in dialysis patients have been reported in several small observational studies ***(Tzamaloukas et al.,1993 &Oomichi et al.,2006)*** , other larger observational studies have found no significant correlation between tight glycemic control and survival ***(Williams et al.,200 &, Duong et al.,2011).***

The HbA1c target that is associated with the best outcome in predialysis CKD patients has not been established. Target HbA1c levels should be tailored to the individual, balancing the improvement in microvascular complications with the risk of hypoglycemia. For most predialysis CKD patients, we suggest using an HbA1c target of approximately 7 percent, although the risks and benefits of targeting this goal are uncertain. Data supporting this goal are from studies of non-CKD patients and are discussed elsewhere (Jeffrey S Berns,et al; 2016). This goal is consistent with the 2012 Kidney Disease Outcomes Quality Initiative (K/DOQI) (National Kidney Foundation, 2012 ) and Kidney Disease: Improving Global Outcomes (KDIGO) (KDIGO ,2013 ) guidelines for patients with CKD. We also agree with K/DOQI and KDIGO that patients who are at risk for hypoglycemia should not be treated to an HbA1c <7 percent and that the target HbA1c may be higher than 7 percent in individuals who have comorbidities or limited life expectancy and who are at risk for hypoglycemia ***(National Kidney Foundation ,2012 &*** KDIGO***,2013).***

Among dialysis patients, target an HbA1c goal of 7 to 8 percent, with the specific goal in individual patients based upon the risk of hypoglycemia and presence of comorbid conditions. For patients who are relatively young (<50 years) and without significant comorbid conditions, we target an HbA1c goal that is close to 7 percent (ie, 7 to 7.5). However, among older patients with multiple comorbid conditions, the HbA1c target is closer to 8 percent (ie, 7.5 to 8).

The A1C is a measure of the irreversible nonenzymatic glycation product of one or both NH2-terminal valines of the β-hemoglobin chain. In ESRF, the A1C assay can be affected by interference from carbamylated hemoglobin formed from urea-derived isocyanate that accumulates in uremia ***(Lee et al., 2002).*** However, advances in reverse-phase cation exchange HPLC analyzers, as used in this study, allow for greater hemoglobin peak separation ***(Schnedl et al.,2005).***

In patients without ESRF, the A1C value is routinely used to assess long-term glycemic control, and assays are standardized to those used in the Diabetes Control and Complications Trial ***(Rohlfing et al.,2002).*** There is a strong correlation between A1C values and the weighted mean glucose values of the preceding 2–3 months ***(Rohlfing et al.,2002).***

The validity of the A1C measurement in patients with ESRF undergoing hemodialysis depends on the methodology (Little RR,et al 2002). A number of factors may influence the assay including altered red blood cell (RBC) life span and metabolic and mechanical factors (Nissenson AR, et al 2002). Potential metabolic factors are interference from carbamylated hemoglobin formed in uremia and acetylated hemoglobin formed from long-term aspirin use ***(Bry et al.,2001).***

Glycated hemoglobin is better than fasting glucose for determining risks of cardiovascular disease and death from any cause ***(Selvin et al.,2010).***

In many diabetic dialysis patients with established DM a decline in insulin requirements and even spontaneous hypoglycemia can also occur ***(Mak,2000)***. The reasons for alterations in glucose homeostasis involve various mechanisms related to both decreased kidney function and dialysis therapies ***(Kalantar-Zadeh et al., 2009)***. Renal clearance of insulin is significantly diminished once GFR declines below 15–20 ml/min ***(Mak,2000).*** Hepatic clearance of insulin also tends to decline in uremia, although it may improve after dialysis initiation ***(Mak,2000).***

Patients with impaired kidney function are prone to hypoglycaemia owing to a delay in the metabolism and excretion of insulin, which is partly degraded in the kidney, and of oral hypoglycaemic agents. Two reports have suggested that most emergency cases of severe hypoglycaemia in patients with substantially impaired kidney function occur in those who have received sulphonylureas or insulin therapy ***(Haneda et al.,2009 & Holstein et al.,2003).***

As in the non-CKD population, the treatment of nondialysis CKD and dialysis patients with diabetes involves both nonpharmacologic and pharmacologic therapies ***(Garg et al.,2013).***

The nonpharmacologic therapies include dietary modification, exercise, and weight reduction. The additional burden of CKD dietary requirements (for example salt, protein, and volume restrictions) may further complicate diets in patients with diabetes ***(Jeffrey Berns et al.,2016) .***

Pharmacologic therapies include insulin and oral agents. Our approach varies depending upon whether patients are on dialysis or not.

This is consistent with the 2005 K/DOQI guidelines, which suggest that, among dialysis patients, newer insulin regimens and insulin preparations should be used rather than oral agents for glycemic control ***(K/DOQI Workgroup,2005).*** This is due to the lack of adequate data concerning the use of oral agents in dialysis patients and their inability to adequately excrete many such agents.

Some clinicians prefer to use oral agents rather than insulin, especially among patients who are already on these agents and have achieved acceptable glycemic control. The preferred agents are glipizide or repaglinide since they are primarily metabolized by the liver, since inactive or only very weakly active metabolites are excreted in the urine, and since the risk of hypoglycemia is lower than with other oral agents ***(Tzamaloukas et al.,2001).***

A consensus approach does not exist to the choice of insulin in patients with diabetes and ESRD ***(Snyder et al.,2004).*** Some suggest that long-acting insulin preparations should be avoided, while others feel that such agents should be used.

Severe hyperglycemia, with serum glucose concentrations occasionally >1000 mg/dL (55 mmol/L), may be observed among dialysis patients with diabetes. Unlike those without ESRD, however, hypovolemia and marked hypernatremia do not occur, since glucosuria is absent in anuric individuals. The net effect is minimal symptoms, even among those with extreme hyperglycemia ***(***Mak,***2000).***

However, these patients may have marked hyperkalemia due to potassium efflux from cells in response to extracellular fluid hypertonicity, as well as hyponatremia and acute intravascular volume expansion ***(***Montoliu ***et al.,1985).***

Hyperglycemia is an important risk factor for the development of microvascular disease in patients with type 2 diabetes, as it is in patients with type 1 diabetes. This has been shown in several observational studies ***(Klein et al.,1994&*** Bash ***et al.,2008).***

Diminished kidney function may affect renal gluconeogenesis (Cano N.2002). The resultant deficient gluconeogenesis combined with impaired renal insulin clearance, uremic malnutrition, and deficient catecholamine release can contribute to a lower than usual threshold for clinical hypoglycemia, which is a common complication associated with adverse outcomes in dialysis patients ***(Arem,1989).***

Hypoglycaemia occurs not infrequently in patients with ESRD, especially during haemodialysis sessions, and is particularly common in those with diabetes mellitus ***(Akmal, 2001 & Jackson et al.,2000 & Simic-Ogrizovic et al 2001) .***

Endogenous production of glucose by glycogenolysis and gluconeogenesis maintains plasma glucose levels during the

fasting state ***(Boden,2004 & Gerich, ,2000& Mather et al.,2011).*** The kidney has sufficient gluconeogenic enzyme and glucose-6-phosphate activity to generate substantial amounts of glucose via endogenous production; renal glucose production is thought to principally occur though gluconeogenesis rather than glycogenolysis (Gerich, J. E,et al; 2001). The kidney contributes to approximately 40% of gluconeogenesis and accounts for up to 20% of all glucose production ***(Meyer et al.,2002).***

Diabetic retinopathy, also known as diabetic eye disease, is when damage occurs to the retina due to diabetes. It can eventually lead to blindness ***(Diabetes.co.uk. 2012).***

It affects up to 80 percent of people who have had diabetes for 20 years or more. ***(Kertes et al.,2007)*** At least 90% of new cases could be reduced if there were proper treatment and monitoring of the eyes. ***(Tapp et al.,2003)*** The longer a person has diabetes, the higher his or her chances of developing diabetic retinopathy. ***(Caroline MacEwen. 2011)*** Each year in the United States, diabetic retinopathy accounts for 12% of all new cases of blindness. It is also the leading cause of blindness for people aged 20 to 64 years. ***(Engelgau, et al 2014).***

We monitor glycemic control in patients with diabetes and predialysis CKD or end-stage renal disease (ESRD) as we do in patients with diabetes and normal kidney function. Thus, we use serial measurements (two to four times yearly) of glycated hemoglobin (hemoglobin HbA1c) to assess chronic glycemic control in diabetic patients with predialysis CKD or ESRD ***(***Jeffrey ***et al.,2016).***

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