Insulin resistance is immediately reduced after hemodialysis sessions in diabetic and nondiabetic patients with end-stage renal disease

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Background
Insulin resistance in patients with end-stage renal disease (ESRD) is a strong independent predictor of cardiovascular death. The effect of hemodialysis sessions on the state of insulin resistance in patients with ESRD was not very clear. The aim of this study was to assess the immediate effect of hemodialysis sessions on insulin resistance in this group of patients.
Patients and methods
This self-control study was carried out at the Alexandria Main University Hospital. The study included 100 patients with ESRD on regular maintenance hemodialysis (50 patients with type 2 diabetes mellitus and 50 patients without diabetes mellitus). Fasting plasma glucose, fasting serum insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), blood urea, serum creatinine, and arterial bicarbonate were assessed before and after the hemodialysis sessions.
Results
Before the hemodialysis sessions, the mean HOMA-IR was 4.58 in patients with diabetes mellitus and 2.37 in patients without diabetes mellitus. The levels decreased significantly to 1.28 in patient with diabetes mellitus ($P<0.001$) and decrease to 0.7 in patient without diabetes mellitus ($P<0.001$) after the hemodialysis sessions. There was a significant negative correlation between HOMA-IR and serum creatinine levels before or after the hemodialysis sessions.
Conclusion
Hemodialysis sessions may cause an immediate improvement in the insulin resistance state in patients with ESRD. The variability of insulin resistance following hemodialysis sessions can lead to marked glycemic fluctuations. Careful monitoring of blood glucose level following hemodialysis sessions may be indicated in some patients with ESRD.

Keywords:
end-stage renal disease, Homeostasis Model Assessment of Insulin Resistance, insulin resistance

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Introduction

Diabetic nephropathy is one of the most serious complications of diabetes mellitus; diabetic kidney disease is responsible for approximately 40% of cases with end-stage renal disease (ESRD) [1–3].

Insulin resistance refers to decreased insulin ability to exert its physiological actions on different insulin-sensitive tissues including the muscles, liver, and adipose tissue. Insulin resistance is not only related to the pathogenesis of type 2 diabetes mellitus (T2DM) but may also have a role in the development of chronic kidney disease [4].

In general, insulin resistance could be a prereceptor resistance, a receptor resistance, or a postreceptor resistance. Insulin resistance in chronic renal disease is mainly related to a postbinding abnormality in insulin action [5–8].

Insulin resistance may lead to kidney damage through altering the renal hemodynamics by mechanisms such as activation of the sympathetic nervous system, sodium retention, and decreased Na+, K+-ATPase activity [9]. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) can be used as an alternative to the hyperinsulinemic-euglycemic glucose clamp to estimate insulin resistance in patients with chronic kidney disease [10–13].

The effect of hemodialysis sessions on the state of insulin resistance in patients with ESRD was not very clear. The aim of this study was to assess the immediate effect of hemodialysis sessions on insulin resistance in this group of patients.

Patients and methods

This self-control study included 100 adult patients with ESRD on regular maintenance hemodialysis (for >6 months, three sessions per week, 4 h session duration) selected from the Alexandria Main University Hospital. On the contrary, patients with morbid obesity (BMI >40 kg/m^2), underweight (BMI<18.5 kg/m^2), type 1 diabetes mellitus, or decompensated liver cirrhosis were excluded.

The studied group was equally divided into two subgroups: subgroup I (50 patients with T2DM) and subgroup II (50 patients without T2DM).

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Alexandria University, Egypt. Signed informed consent was obtained from each patient before any study-related activities [10].

Patients were asked to fast for 8 h before the hemodialysis session and to continue fasting till the end of the session. Blood urea, serum creatinine, arterial bicarbonate, fasting plasma glucose, and fasting serum insulin were measured just before the hemodialysis sessions and repeated immediately after the hemodialysis session. Insulin resistance was calculated by HOMA-IR using the formula: fasting serum insulin (μUml)×fasting plasma glucose (mmol/l)/22.5 [10].

Data were analyzed by using Student's *t* test (paired and unpaired) and Pearson's correlation coefficient (*r*).

Results

Descriptive statistical data of the studied patients

The study included 100 patients with ESRD. The mean age of the studied patients was 49.7 years, the mean BMI was 25.2 kg/m^2, and the mean duration for which the patients were on regular hemodialysis was 53 months (Table 1).

Table 1 Descriptive statistical data of the studied patients (*N*=100 patients)

	Minimum	Maximum	Mean	SD
Age (years)	33.0	71.0	49.7	8.9
Weight (kg)	48.0	87.0	69.2	8.9
BMI (kg/m^2)	17.6	33.6	25.2	3.3
SBP (mmHg)	110.0	175.0	136.5	16.2
DBP (mmHg)	70.0	110.0	85.2	9.6
Duration of hemodialysis (months)	47.0	62.0	53.0	4.1

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Blood urea

The mean of blood urea levels significantly decreased from 101.2 mg/dl before hemodialysis sessions to 62.7 mg/dl after the hemodialysis sessions (*P*=0.013).

Serum creatinine

The mean of serum creatinine levels significantly decreased from 10.0 mg/dl before hemodialysis sessions to 6.1 mg/dl after the hemodialysis sessions (*P*=0.011).

Arterial bicarbonate

The mean arterial bicarbonate levels significantly increased from 19.5 mmol/l before hemodialysis sessions to 24.5 mmol/l after the hemodialysis sessions (*P*=0.038).

Fasting plasma glucose level

In subgroup I, the mean fasting plasma glucose level was 127.38 mg/dl before hemodialysis sessions and 96.62 mg/dl after the hemodialysis sessions (*P*<0.001).

In subgroup II, the mean fasting plasma glucose level was 88.48 mg/dl before hemodialysis sessions and 78.96 mg/dl after the hemodialysis sessions (*P*<0.001).

Fasting serum insulin

In the 100 studied patients, the mean fasting serum insulin level significantly decreased (*P*=0.001) from 14.2 μU/ml before hemodialysis sessions to 4.6 μU/ml just after the hemodialysis sessions (Table 2).

In the subgroup I, the mean fasting serum insulin level significantly decreased (*P*=0.001) from 17.3 μU/ml before hemodialysis sessions to 5.45 μU/ml just after the hemodialysis sessions.

In the subgroup II, the mean fasting serum insulin level significantly decreased (*P*=0.001) from 11.18 μU/ml before hemodialysis sessions to 3.64 μU/ml just after the hemodialysis sessions.

Homeostasis Model Assessment of Insulin Resistance

In the 100 studied patients, the mean HOMA-IR level significantly decreased (*P*=0.0074) from 3.5 before hemodialysis sessions to 1.0 just after the hemodialysis sessions (Table 2).

In comparison between the two studied subgroups, in subgroup I, HOMA-IR before hemodialysis ranged between 0.94 and 16.32, with a mean value of 4.58 ±3.37, and in subgroup II ranged between 0.58 and 5, with a mean value of 2.37±1.16. However, in subgroup I, HOMA-IR after hemodialysis ranged between 0.71 and 3.76, with a mean value of 1.28±0.66, and in subgroup II, ranged between 0.17 and 1.70, with a mean value of 0.70±0.37. There was a statistically significant decrease in HOMA-IR just after the hemodialysis sessions in both subgroups ($P<0.05$) (Fig. 1).

There was a significant positive correlation between HOMA-IR before hemodialysis sessions and creatinine level before hemodialysis sessions ($r=0.225$, $P=0.024$) (Fig. 2), and also there was a significant positive correlation between HOMA-IR levels after the hemodialysis sessions and creatinine levels just after the hemodialysis sessions ($r=286$, $P=0.004$) (Fig. 3).

Table 2 Fasting serum insulin level, fasting glucose level, and Homeostasis Model Assessment of Insulin Resistance before and after hemodialysis in the studied patients (*N*=100 patients)

	Before HD	After HD	*P*
Insulin (μU/ml)			
Range	2.5–28.0	1.0–13.3	
Mean	14.2	4.6	0.001*
SD	7.5	2.4	
Glucose (mg/dl)			
Range	74.0–210.0	51.0–174.0	
Mean	107.9	87.8	0.015*
SD	33.5	19.1	
HOMA-IR			
Range	0.6–16.3	0.2–3.8	
Mean	3.5	1.0	0.0074*
SD	2.7	0.6	

HD, hemodialysis; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance. *Statistical significance.

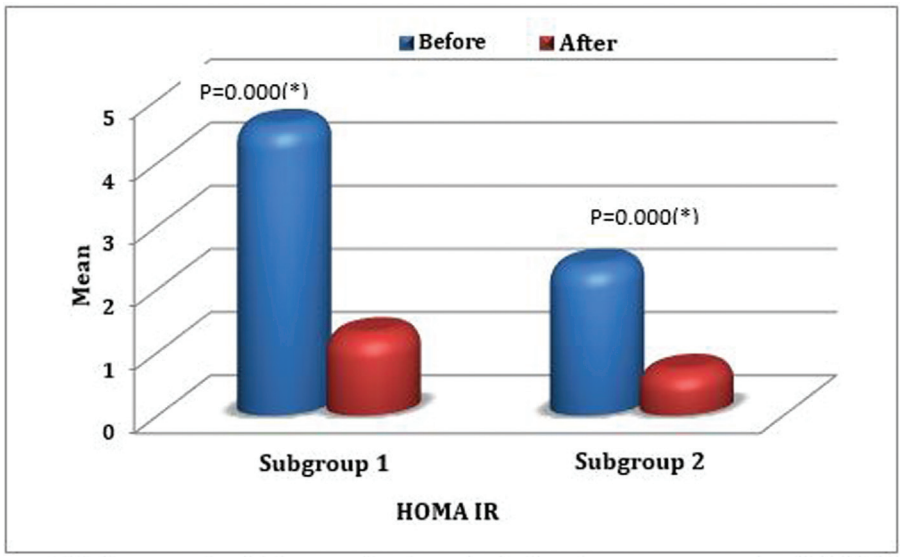
Discussion

Insulin resistance is a characteristic feature of ESRD. Different mechanisms are implicated in the pathogenesis of insulin resistance in ESRD, including low physical activity levels, toxins of the uremic state, metabolic acidosis, electrolyte disturbance, chronic inflammatory state, oxidative stress, vitamin D deficiency, and abnormal adipokines levels, leading to a postinsulin-receptor defect in different insulin-sensitive tissues [14–16].

In this present study, there was a significant decrease in fasting serum insulin levels after hemodialysis sessions in the studied patients regardless of whether they had T2DM or not; this was previously reported by Nad *et al.* [17] who found that the serum insulin levels significantly decreased after hemodialysis in the diabetic and nondiabetic patients.

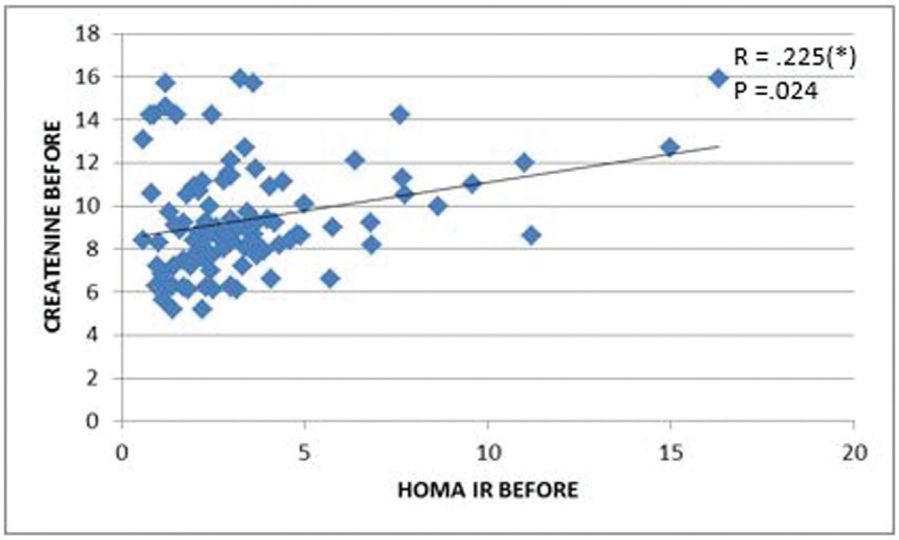
The reduction in fasting serum insulin levels after hemodialysis sessions may be explained by improvement of insulin resistance or by greater insulin clearance on the dialysis day, although insulin is poorly dialyzed [18].

Figure 1



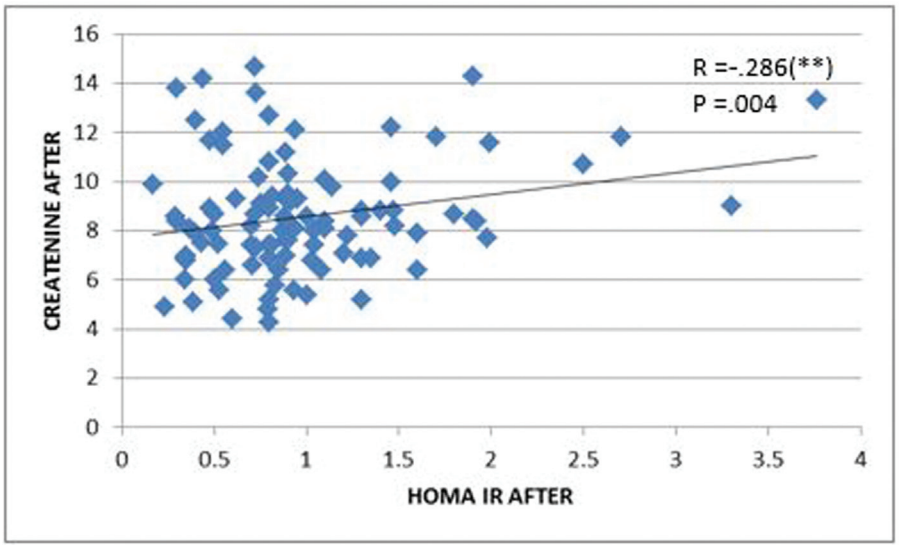
Comparison between the two studied subgroups regarding HOMA-IR. HOMA-IR, Homeostasis Model Assessment of Insulin Resistance. *Statistical significance.

Figure 2



Correlation between HOMA-IR and creatinine before hemodialysis. HOMA-IR, Homeostasis Model Assessment of Insulin Resistance. *Statistical significance.

Figure 3



Correlation between HOMA-IR and serum creatinine after hemodialysis. HOMA-IR, Homeostasis Model Assessment of Insulin Resistance.

The main finding of our study was the significant improvement in insulin resistance immediately after the hemodialysis sessions even in patients without T2DM. The reduction in insulin resistance following the hemodialysis sessions may explain the results of Sobngwi *et al*. [18] who reported significant (25%) reduction in basal insulin requirements the day after hemodialysis when compared with the day before.

The opposing effects of ESRD and hemodialysis on insulin resistance may cause marked swings in blood glucose levels in patients with ESRD, placing patients at risk of hypoglycemia and presenting a challenge for nephrologists and diabetologists [18–20].Another important finding of our work is the significant positive correlation between HOMA-IR and serum creatinine levels. Similarly, Kobayashi *et al*. [1] found that insulin resistance is correlated linearly with decline in renal functions. Although uremic toxins may be one of the factors that lead to insulin resistance in patients with ESRD, the specific uremic toxin leading to this abnormality is not yet fully identified [15].

Conclusion

Hemodialysis sessions may cause an immediate improvement in the insulin resistance state in patients with ESRD. The variability of insulin resistance following hemodialysis sessions can lead to marked glycemic fluctuations. Careful monitoring of blood glucose level following hemodialysis sessions may be indicated in some patients to with ESRD.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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