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Assessment of Pulmonary Function in End Stage Renal Disease Patients on Regular Hemodialysis

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ABSTRACT

Background: end-stage renal disease (ESRD), is the last stage of chronic kidney disease. When your kidneys fail, it means they have stopped working well enough for you to survive without dialysis or a kidney transplant.
Objective: it was to assess the pulmonary function in patients with ESRD after hemodialysis.
Patients and Methods: Prospective study which was done in tertiary level care center.Thirty ESRD patients who were on hemodialysis regularly were studied.
Results: The mean FEV1/FVC% which was observed in the patients of this study was 67.8±20.8% of the predicted value, after hemodialysis, the mean FEV1/FVC% increased up to 82.3±20.1% of the predicted value, and this increase was statistically significant with P value <0.006. The mean of the forced expiratory flow 25-75% (FEF 25-75%) of the studied patients pre-dialysis was 53.1±33% of the predicted value, after hemodialysis, the mean of the FEF 25-75% increased up to 58.3±34.6% of the predicted value and that was statistically significant with P value <0.05. The mean of the peaked expiratory flow rate (PEFR) was 47.8±31.7% of the predicted value and after hemodialysis, the mean PEFR increased to 52.1±30.9% of the predicted value and that was statistically significant with P value <0.05).
Conclusions: pulmonary function tests decrease significantly among ESRD patients who undergo hemodialysis regularly pre and after the sessions of hemodialysis. Most ESRD patients were with abnormal pulmonary functions, mainly of a restrictive pattern.
Keywords: ESRD, Regular Hemodialysis.

INTRODUCTION

End stage renal disease (ESRD) is irreversible and progressive disease which characterized by irreversible loss of kidney function. The ESRD is terminal and final pathway that resulted eventually in most of the patients suffering from medical problems affecting their renal function. Patients with ESRD need renal replacement therapy once they are established the ESRD stage via and that may either be achieved by dialysis (hemodialysis or peritoneal dialysis) or need kidney transplantation so as to be able to keep functioning normal renal life. There was an observed increase in the morbidity and mortality in ESRD patients because of the presence of the renal replacement therapy (HD or renal transplantation). Despite that ESRD may appear as a single organ dysfunction, it also affects multiple organs with variable and numerous complications which resulted in multi-organ dysfunction so the systemic complications presented in ESRD patients are very important [(1)].

One of the most important of these complications is the respiratory system dysfunction related to renal dysfunction which is a very common complication in ESRD patients [(2)]. Rising in the blood urea level, may be the cause that affects the respiratory system in the form of pulmonary edema, pleural effusion and acute respiratory distress syndrome (ARDS) [(3)].

Directly or indirectly, renal failure affects mechanical and ventilatory functions of lung and also drugs and hemodialysis (HD) contribute to the change in air flow [(4)]. Pulmonary renal syndrome is a group of diseases that affects both the pulmonary and the renal functions [(5,6)]. The most presenting symptom of these syndromes is hemoptysis from diffuse alveolar hemorrhage, along with renal insufficiency associated with either acute glomerulonephritis or other vasculitis. However, patients may develop alveolar hemorrhage without presence of renal involvement, which may appear later[(5)].

Many of these disorders such as Wegener's granulomatosis, Microscopic poly-angitis, mixed cryo-globulinemia, Henoch-Scho¨nleinpurpura, immune-complex-associated, Good-Pasture syndrome and SLE.

The deteriorated pulmonary function may be attributed to the effect of the circulating toxins from the renal uremia or indirectly as an effect from the increased fluid load, immune response, electrolyte imbalance, anemia, malnutrition, and/or acid-base disturbance[(7)]. The increased of body fluid is a serious and very common problem which may cause serious complications in HD patients.

In the inter-dialytic period, weight differences are commonly seen in ESRD patients on the regular hemodialysis may be attributed to the increased body fluid load [(8)]. The increased fluid load, Permeability of the pulmonary capillary may increase, which can lead to pulmonary edema and pleural effusion; such abnormalities can explicate the reducedpulmonary normal function [(9, 10)].

Since hemodialysis clears the increased body fluid and the uremic toxins, this can be the cause of the improvement of the pulmonary functions by reducing water content of the lungs and excreting the excess toxins resulted from uremia. Many mechanisms may be the cause of the deteriorated pulmonary function and the altered bronchial responsiveness presented in ESRD

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patients on long term regular hemodialysis, some of these mechanisms are increased lung extra-vascular water, trapped neutrophils, left ventricular hypertrophy, calcification, metastatic lung, and iron deposition[11, 12].

The respiratory muscles, the main ones as the diaphragm and the accessory ones as inter-costal muscles may show weakness of these muscles as a result of the uremic syndrome accompanying the ESRD patients. Some researchers[13] who had done researches on the effects of uremia on the respiratory muscles had the conclusion that severe uremia may be the cause of the decrease in these muscles' strength.

The ventilatory defect as a result of this deterioration in respiratory muscles function, along with other lung tissue deterioration, leading to the declining of the functional advantage of the respiratory system, which can be attributedthe decrease of the lung capacity [14,15]. During hemodialysis, many of our studied patients have a reduction in arterial PO2.

The arterial PO2 falls within a few minutes after the initiation of the dialysis by 8-12 mmHg, reaches a nadir after 40-80 min, and persisted for the entire duration of the procedure [16].

Several mechanisms can expound the declineof the arterial PO2:

(1) Alkalosis or acidosis which may cause respiratory center depression.

(2) Severe acidosis or alkalosis which may affect the oxygen dissociation curve.

(3) Presence of leucocytes cells in the smaller blood vessels of the pulmonary tree may lead to ventilation perfusion disturbance.

(4) Excretion of CO2 during dialysis may cause impairment in the oxygen diffusion and hypoventilation.

AIM OF THE WORK

It was to assess the pulmonary function in patients with ESRD after hemodialysis.

PATIENTS AND METHODS

We held our study prospectively in a tertiary care center and it was carried out over six months' period from October 2018 to April 2019.

This study was carried out on 30 ESRD patients undergoing regular HD. **The study was given the approval by Al-Azhar University Ethics Committee concerning researches.**

Inclusion criteria: Stable patients who were determined based on the clinical dataand who aging 18-60 years, who were undergoing HD for at least three months, were added to this study.

Exclusion criteria: Patients with signs or symptoms suggesting acute infection, acute kidney failure, patients who were unable to do spirometry due to that they have severe respiratory distress, chronic pulmonary disease, tuberculosis, heart failure, arrhythmias, liver cirrhosis, skeletal muscle deformities, and or anyonewho was unable to perform well during spirometry testing couldn't be added to this study.

Informed consent from all patients after informing them about the specifications of the study was obtained from the studied patients while the study was running. Individuals' data were written down on an assessment form. The glomerular filtration rate (GFR) was estimated using the empirical formula for creatinine clearance (Cockcroft-Gault equation).

Spirometric pulmonary function tests were done using a computerized spirometer immediately before and after the mid-week hemodialysis session of all patients. All patients were able to conduct acceptable and re-producible forced expiratory maneuvers by the same physician. The patients were doing the test in a sitting position while putting on a nose clip using standard parameters to perform such tests.

Forced vital capacity (FVC), forced expiratory volume in the 1st second (FEV1), peak expiratory flow rate (PEFR), mean forced expiratory flow between 25% and 75% of the FVC (FEF25–75), and the FEV1/FVC ratio were measured and calculated as% predicted using normal values based on age, race, height, and sex (FVC%, FEV1%, PEFR%, and FEF 25–75%). Spirometric parameters were recorded 15 minutes before and after the HD session. Routine laboratory tests were done as CBC, creatinine, blood urea, serum calcium and serum phosphorus, ABG, LFTs, serum lactate and RBS.

Analysis of the obtained data was done using the Statistical Package for Social Sciences (SPSS), Windows version 18.0 (SPSS Inc., Chicago, IL). The variables collected data were illustrated using visual (probability plots and histograms) and analytical (Kolmogorov-Smirnov test) ways.

Normally the obtained variables were presented as means ± standard deviations. P values <0.05 were computedas statistically significant.

Examinations of ESRD patients were carried out during the middle week session. The dialysis were performed by the Fresenius 4008-S a German machine. All patients had a dialysate fluid of 1.7 m2 surface area with high-flux polysulphone dialyzers (Fresenius, Bad Homberg, Germany) with bicarbonate-based dialysate (Glucose 1 mmol/L, Na+ 140 mEq/L, HCO3–32 mEq/L, K+ 2.0 mEq/L, Ca2+ 1.25 mmol/L, Mg2+ 0.5 mEq/L). The duration of the sessions was 240 minute with a blood flow rate of 250–350 ml/min and dialysate flow rate of 500 ml/min.

All patients' data concerning the demographics and baseline clinical characteristics were obtained from patients themselves or patients' registries. BMI was calculated using the weight/height2 (kg/m2) equation. Samples of the patients' blood were collected pre and after dialysis for the biochemical and hematological investigations.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc.,

Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
- Probability (P-value)
- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

RESULTS

All patients' data concerning clinical characteristics (Table1) such as age, sex, height, weight and BMI were recorded as follow; the mean group age of the study patients was 45.23 ± 11.1 years (range 24 to 60 years), 60% of the studied patients were below fifty years of age.

The females were the dominant number of this study with sixteen cases (53%).

The mean height of the studied patients was 169.9±8.6 cm. 64% of the studied patients were from a rural background. The mean weight of the studied patients post-dialysis was 71.3±15.5 Kg, 43.3% of the studied patients had a normal BMI (Table 2).

On investigation; CBC, serum creatinine, urea and LFTs were done and recorded (Table 3).

All patients were anemic (hemoglobin < 12 g %), the hemoglobin values ranged from 5.8 to 11.6 g/dl (mean ± standard deviation, SD: 9.2± 1.6 g/dL) among all the patients. The WBCs count ranged from 3200 to 9700 cell /dl (mean ± standard deviation, SD 6650± 1900 cell /dL) among all the patients.

The platelets count ranged from 155000 to 389000 cell /dl (mean ± standard deviation, SD 248900± 80100 cell /dL) among all the patients. The serum albumin ranged from 3.3 to 4.99 gm/dl (the mean was 4.37 ± 1.1 gm/dL) while the serum bilirubin levels ranged from 0.2 to 1.2 mg/dl (the mean was 0.56± 0.18 mg/dL).

The ALT ranged from 7 to 44 U/L (mean ± standard deviation, SD 19± 11 U /L) The AST ranged from 7 to 43 U/L (mean ± standard deviation, SD 21± 13 U /L).

Pre-dialysis serum urea levels ranged from 19 to 141 mg/dl (89.2± 26.16 mg/dl). Post-dialysis serum urea levels ranged from 8 to 73 mg/dl (43.1± 15.4 mg/dl).

Serum creatinine ranged from 2.4 to17.7 mg/dl (10.85 ± 4.3 mg/dL) and estimated GFR 3.0-19.8 ml/min/1.73 m2 (7.8 ± 3.4 ml/min/1.73 m2).

60% 0f studied patients were on hemodialysis from 6 months-5years and 10 were females and 8 were males (Table 4). The majority (60%) of the studied patients were doing hemodialysis three times per week, while 30% of the studied patients were doing hemodialysistwo timesper week. Ten% of the studied patients were doing hemodialysis one timeper week (Table 5).

Diabetes mellitus (10%), hypertension (36.67%) analgesic abuse and congenital renal atrophy were each (13.3%).

FVC%: The mean FVC% of the studied patients was 47.8 ± 27.9% of predicted value, which was below the normal predicted values for pulmonary function (normal is > 80% of the predicted values). After HD, this mean increased to 56.1 ± 29.4% of predicted value, and this increase was statistically highly significant (P less than 0.01) (Table 4).

FEV1%: The mean FEV1% of the studied patients was 39.5 ± 22.9% of predicted value, which was also below the normal predicted values (normal is > 80% of the predicted values). After HD, this mean increased to 47.3 ± 28.5% of predicted value, and this increase was statistically highly significant (P less than 0.01) (Table 6).

FEV1/FVC%: The mean FEV1/FVC% of the studied patients was 67.8 ± 20.8% pred. After HD, the mean FEV1/FVC% increased to 82.3 ± 20.1% of predicted value, and this increase was statistically significant (P less than 0.05) (Table 6).

Forced expiratory flow (FEF) 25-75%: The mean FEF 25-75% of the studied patients was 53.1 ± 33% pred. After HD, this mean increased to 58.3 ± 34.6% of the predicted value, and this increase was statistically significant (P less than 0.05) (Table 6).

Peak expiratory flow rate% (PEFR %): The mean PEFR of the studied patients was 47.8 ± 31.7% of predicted value, i.e. below the normal range (normal are >80% of predicted values). After HD, the mean PEFR increased to be 52.1 ± 30.9% of predicted value, and this increase was statistically significant (P less than 0.05) (Table 6).

Table (1): Characteristics data of the 30 patients with ESRD on regular HD

Data	Mean ± SD
Age	45.23 ± 11.1 year
Sex; Females (F) : Males (M)	16 F : 14 M (53% : 47)
Weight	71.3±15.5 Kg
Height	169.9±8.6 cm

Table (2): Body mass index status of study patients (in kg/m2)

Body mass index (kg/m2)	No. of patients (n)	(%)
Underweight (< 18.5)	1	3.33
Normal (18.5-24.99)	13	43.33
Overweight (25-29.99)	8	26.67
Obese (> 30)	8	26.67

Table (3): CBC, LFTs, and KFTs collected data from all 30 patients

Data	Mean ± SD
Hemoglobin	9.2± 1.6 g/dL
WBCs	6650± 1900 cell /dL
Platelets	248900± 80100 cell /dL
Albumin	4.37 ± 1.1 gm/dL
Bilirubin	0.56± 0.24 mg/dL
ALT	19± 11 U /L
AST	21± 13 U /L
creatinine	10.85 ± 4.3 mg/dL
Urea pre-dialysis	89.2± 26.16 mg/dl
Urea post-dialysis	43.1± 15.4 mg/dl

Table (4): Duration of hemodialysis among study patients

Duration of hemodialysis	Females (n = 16)	Males (n = 14)	Total (n = 30)	%
< Six months	**0**	3	3	10
Six months- 1 year	**1**	0	1	3.33
1 year- 5 years	**9**	8	17	56.67
> 5 years	**6**	3	9	30

Table (5): Frequency of hemodialysis among study patients

Frequency of hemodialysis	Total (n=30)	%
Once a week	3	10
Twice a week	9	30
3 times a week	18	60

Table (6): Predicted spirometric parameters in% in the study patients (before and after hemodialysis {HD}) (n = 30)

Spirometric parameters	Before HD (mean ± SD)	After HD (mean ± SD)	P-Value
FVC%	7.8 ± 27.9%	56.1 ± 29.4%	< 0.001
FEV1%	39.5 ± 22.9%	47.3 ± 28.5%	< 0.001
FEV1 / FVC (%)	67.8 ± 20.8%	82.3 ± 20.1%	0.0052
FEF 25-75%	53.1 ± 33%	58.3 ± 34.6%	0.043
PEF%	47.8 ± 31.7%	52.1 ± 30.9%	0.006

DISCUSSION

The mean age of our studied patients was 45.23 ± 11.1 years and 60% of those patients were below 50 years, thus suggesting that CKD had emerged as an early complication of various disorders.

The most of our studied patients were females (53%) which may have reflected either greater prevalence of CKD among females or poor availability of highly cost of the regular hemodialysis treatment for male patients. The mean BMI of the studied patients was 26.08 ± 4.4 kg/m2 and 43.33% had BMI of 18.5-24.99 kg/m2, but the majority (53.34%) of the studied patients had above normal BMI. This was despite chronic illness, but the patients' obvious water retention and edema may have led to their abnormal BMI.

Anemia was present in all patients; this may be due to the chronicity of the renal disease our patients have and malnutrition they may also have, which reflecting as an inflammatory state and malnutritional status among our studied patients. Most of these circumstances may also be as a cause of the hyper-catabolic state among the ESRD patients, caused by a multiple factors as uremic toxicity or accumulation of pro-inflammatory cytokines, insulin resistance and lack amino acid [17] during the session of hemodialysis, it is also may be due to insufficient high protein diet [18].

In our study we observed that there were statically significant differences between Pre and post hemodialysis spirometric parameters as FVC%, FEV1%, FEV1/FVC%, FEF25-75% and PEF%.

FVC%: The pre-dialysis mean FVC±SD% of predicted value of our studied patients was 47.8 ± 27.9% of predicted value and it was increased post-dialysis to 56.1 ± 29.4% of predicted value with P-Value < 0.001 and that was statistically significant and this findings regarding FVC are in consistent with **Mahmoud *et al.*[19]** and **Davenport *et al.*[20]**. These findings may be explained by the chronic subclinical pulmonary edema as a result of the increased pro-inflammatory cytokines and the increased capillary permeability and why that was improving after HD [21, 22].

FEV1%: The pre-dialysis mean FEV1±SD% of predicted value of our studied patients 39.5 ± 22.9%of predicted value and it was increased post-dialysis to 47.3 ± 28.5% of predicted value with P-Value < 0.001 and that was statistically significant.

Reduced FEV1% which was seen in our study was has also acknowledged by **Mahmoud *et al.*[19]** and **Nascimento *et al.*[23]** and that may be because of the inflammatory state and inadequate nutrition which have been observed as a significant relationships with decreased pulmonary parameters [20].

FEV1/FVC%: The pre-dialysis mean FEV1/FVC±SD% of predicted value of the studied patients 67.8 ± 20.8% of predicted value and it was increased post-dialysis to 82.3 ± 20.1% of predicted value with P-Value = 0.0052 and that was statistically significant.

Regarding FEV1% and FVC%, there were significant changes in the studied patients concerning the FEV1/FVC% ratio after hemodialysis, because there was parallel increase in both of these parameters (FVC% and FEV1%) but more significantly in FEV1% which may be because of the wash of the excess fluid which reflected on the intra-alveolar fluid or edema which may be because of the volume overload or the increased capillary permeability.

FEF 25-75%: The pre-dialysis mean FEF 25-75±SD% of predicted value of the studied patients 53.1 ± 33% of predicted value and it was increased post-dialysis to 58.3

± 34.6% of predicted value with P-Value = 0.043 and that was statistically significant. These values were also seen in **Mahmoud *et al.*[19]**who also observed decreased values which indicated the existence of small airway disease [19]. This increase in the FEF 25-75% that was achieved through the hemodialysis in our studied patients indicated that these conditions were reversible obstruction and with the removal of the overloaded fluid from those patients' lungs which was chocking the small airways. Despite that, the chronic subclinical pulmonary edema leading to peri-bronchial fibrosis may also be the cause of the persistent abnormalities in the smaller airways which were reflected over the reduced FEF 25-75% values.

PEFR: The pre-dialysis mean PEFR±SD% of predicted value of the studied patients 47.8 ± 31.7% of predicted value and it was increased post-dialysis to 52.1 ± 30.9% of predicted value with P-Value = 0.006 and that was statistically significant.

These values were also seen in **Mahmoud *et al.*[19]** who also observed decreased values which indicated the existence of small airway disease. Reduced PEFR before and even during HD sessions was observed by Davenport, who said that this may be because of the activation of the complement system for neutrophils, platelets and monocytes following blood membrane interaction, resulting in observable airway constriction [24]. Contrasted the findings from our study, normal PEFR values were observed by **Lang *et al.*[25]**.

CONCLUSION

The abnormalities detected in the pulmonary function were seen commonly in our studied patients were significantly improved after the hemodialysis. Most of our studied patients had restrictive respiratory disorders and mixed constrictive and obstructive.

Spirometric parameters as FVC, FEV1, FEF25-75% and PEFR% were < the normal predicted values in most of these patients. In comparing the pre-hemodialysis and post-hemodialysis spirometric parameters, there was significant increase but normal predicted values were still not achieved.

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