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# Pulmonary hypertension and right-sided heart failure in hemodialysis patients

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## Abstract

**Background & Objectives:** Cardiovascular complications are associated with poor outcomes in patients with End stage renal disease. This study is aimed to evaluate the prevalence of pulmonary hypertension and right side heart failure in hemodialysis patients, trying to decrease these complications by referring them to the cardiologist in order to manage them either by medical or interventional methods.

**Methods:** A cross-sectional study for evaluation the prevalence of pulmonary hypertension and right sided heart failure in hemodialysis patients was carried out in Duhok kidney center in Kurdistan region-Iraq through a duration period of one year from first of February, 2020 to 31st of January, 2021 for 101 patients. Data were collected which included Age, gender, BMI, causes of renal failure and vascular access, and echocardiography was conducted by a cardiologist, he evaluated them by using tricuspid regurgitation jet peak gradient for pulmonary hypertension, and by using tricuspid annulus plane systolic excursion method for evaluation of right ventricular function.

**Results**: In the current study 51 females with melasma. Their ages ranged between (19-46) years, with (59.9%) between (28-38) years. The duration of melasma was from 6 months to 9 years. Thirty-eight of them were married and had pregnancy. Thyroid stimulating hormone levels were high in 22 of them (43.1%), 20 out of 22 cases that was had high levels of thyroid stimulating hormone had dermal type of melasma by Wood's lamp examination and their p-value was significant (0.001).

**Conclusion:** The prevalence of pulmonary hypertension among patients on hemodialysis in Kurdistan region-Iraq is within the Iraqi and international range studies with low prevalence of right ventricular dysfunction.

**Key words**: End-stage renal disease, Hemodialysis, Pulmonary hypertension, Right-sided heart failure.

## Introduction

Pulmonary Hypertension (PHT) is characterized by pulmonary artery pressure more than 30 mmHg by echocardiography.[1] Causes of PHT might be idiopathic or due to other medical disorders,Pulmonary hypertension is classified currently into five groups; pulmonary arterial hypertension, pulmonary hypertension related to left-sided heart disease, pulmonary hypertension related to chronic lung disease and/or chronic hypoxia, chronic thromboembolic pulmonary hypertension and pulmonary hypertension with

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unknown etiology.[2] Generally, PHT is accompanied with high morbidity and mortality rates, shorter survival and high burden on national health institutes.[3-5] Higher morbidity and mortality outcomes of PHT are attributed to the effect of pulmonary hemodynamic dysfunctions on renal system.[6] pulmonary hypertension is commonly related to end-stage renal disease (ESRD).[6]It was shown that the prevalence of PHT in patients with renal dysfunction was (21%) that increased gradually to (32.8%) among patients with ESRD[7]. However, the prevalence of PHT is reaching to (65%) among ESRD patients on dialysis.[8] Different mechanisms are reported in pathophysiology of PHT in chronic kidney disease (CKD) patients like the induction of pulmonary venous hypertension through increased blood flow which is attributed to chronic volume overload and increased volume preload in CKD patients that affect the left ventricular (LV) function. Additionally, the effect of higher blood pressure related to CKD might lead to PHT[9]Several risk factors have a role in PHT in CKD patients including Sleep apnea, LV dysfunction, arteriovenous fistula (AVF) and effectiveness of endogenous vasoconstrictor and vasodilator substance.[9] Also; other risk factors related to PHT in patients with ESRD are age, hemoglobin level, LV ejection fraction and left ventricular hypertrophy (LVH).[7] Right ventricular (RV)failure is mostly attributed to LV dysfunction by higher pressure and increased volume overload.[10] The ESRD patients on hemodialysis (HD) have the higher risk of concordance with PHT and right sided heart failure with poor prognosis.[11] Pulmonary hypertension is related with high catecholamine level and activation of renin aldosterone system and is attributed to RV dysfunction.[12, 13] To acquire better outcomes of HD, effective strategies in diagnosis, treatment and prevention of heart diseases during HD are needed.[11]This study aimed to evaluate the incidence of PHT and RV dysfunction in HD patients in Duhok kidney center in Kurdistan region-Iraq that may need to refer the patients with these medical complications to the cardiologist to manage them either by medical or interventional methods to decrease the cardiovascular complications among the patients on HD

## Materials and methods

Our study was carried out in Sulaymaniyah shahid jabar shekh fatah dermatology teaching center in Sulaymaniyah city, Kurdistan Region – Iraq. After acceptance of our research protocol by ethical and scientific committees of Kurdistan board for medical specialties on fifty one patients, which were all females during a period of five months from November 2019 to February 2020 in a prospective cross-sectional study design because during this period we don't have any male patient present with melasma. After taking of verbal consent from each patient, detailed history regarding identity, age, gender, melasma risk factors, its first appearance and its period were all taken. The diagnosis of melasma was done clinically on experience of two board certified dermatologists after that, the patient was sent to investigation of the levels of serum triiodothyronine (T3), thyroxine (T4) and thyroid-stimulating hormone (TSH), along with clinical assessment by Wood's light examination to discover the sort of the melasma. Normal values were considered as: T3= (1.3-3.1 nMol/L), T4= (66-180 nMol/L), TSH= (0.4-4.0 mIU/L). After data collection and prior to data entry and analysis, the questions of study were coded. Data entry performed via using an excel spreadsheet then the statistical analysis was performed by SPSS program, version 21 (IBM SPSS Statistical Package for the Social Sciences). Compliance of

quantitative random variables with Gaussian curve (normal distribution) was analyzed using Kolmogorov-smirnov test. The data presented in tabular forms showing the frequency and relative frequency distribution of different variables among the all three groups of patients (Dermal, Epidermal and Mixed). Chi-square tests were used to compare the categorical data between these groups in respect to normality of thyroid hormones. Different types of Bar charts, Box plots and Error bars were used to describe the study variables diagrammatically.For quantitative variables as T3, T4 and TSH which shown to be not normally distributed so after comparing the mean and standard deviation of these variables (T3, T4 and TSH) among different types of study group (melasma groups) by using ANOVA test, Kruskal Wallis test also been used to compare their median and mean ranks, p-values < 0.05 were used as a cut off point for significance of statistical tests.

## Patients and methods

The current study design was a cross-sectional study that was carried out in Duhok kidney center in Kurdistan region-Iraq through a duration period of one year from first of February, 2020 to 31st of January, 2021. The study population was the patients with end-stage renal diseases (ESRD) on Maintenance HD. Adult patients (age ≥18 years) with ESRD, on regular HD for six months at least were the inclusion criteria. Exclusion criteria were chronic lung diseases, connective tissue diseases, and congenital heart diseases. The ethical considerations were implemented according to the Helsinki Declaration regarding ethical approval of Health authorities; ethical approval was obtained from Kurdistan Board Ethical Committee and confidentiality of data on 27th of October 2020. A convenient sample of 101 patients on HD was selected after eligibility to inclusion and exclusion criteria. The data were collected by the researcher including Age, gender, BMI, causes of renal failure and vascular access and with echocardiography findings which were evaluated by cardiologist. Trans-thoracic echocardiography was conducted by a cardiologist in the Heart Center. By using the Vivid E9 echo machine, we evaluated patients on HD for PHT and RV dysfunction by using TR jet peak gradient and TAPSE respectively. Gradient of 30mmHg and more is considered pulmonary hypertension, 30mmHg to 45mmHg is considered mild pulmonary hypertension, 45mmHg to 65mmHg is moderate pulmonary hypertension and more than 65mmHg is considered severe pulmonary hypertension1. TAPSE (tricuspid annulus plane systolic excursion) correlates closely with the RV function.The general characteristics of patients with regular HD were presented in number (percentage) and in mean (Sta. deviation). Echocardiography findings were presented in number(percentage). The prevalence of PHT and right side heart failure in HD patients was determined in number (percentage). The comparisons of general characteristics in patients with and without PHT were examined in one-way ANOVA and Pearson Chi-squared tests. The comparisons of echo findings in patients with and without PHT was examined in a chi-squared test. The significant level of difference was determined in a p-value of less than 0.05. The statistical calculations were performed in SAS JMP Pro 14.3.

## Results

This study included 101 patients on maintenance HD 2 to 3 sessions per week every session duration about 3and half hour to 4 hours. The mean age of the patients was 48.4 (SD: 15.7) between 19 and 90 years. The average BMI of the patients was 22.3 (SD: 3.4) from 17.6 to 24.5. The patients were males (53.5%) and females (46.5%). Diabetes mellitus (DM) was the most prevalent cause of renal failure (16.8%) followed by HT (12.9%). The vascular access in patients was arteriovenous fistula (AVF) (32.7%) and central venous (CV) line (67.3%), Table(1).

**Table (1):** General characteristics of patients with regular hemodialysis.

| Characteristics (n=101) | Frequency distribution | |
|---|---|---|
| | Mean | SD |
| Age (Range: 19-90 yrs.); Mean (SD) | 48.4 | 15.7 |
| BMI (Range: 17.6-24.5); Mean (SD) | 22.3 | 3.4 |
| | Number | percentage |
| Gender; no (%) | | |
| Male | 54 | 53.5 |
| Female | 47 | 46.5 |
| Causes of renal failure; no (%) | | |
| Diabetes Mellitus | 17 | 16.8 |
| Glomerulonephritis | 1 | 1.00 |
| Hypertension | 13 | 12.9 |
| Other factors | 69 | 68.3 |
| Vascular access; no (%) | | |
| AVF | 33 | 32.7 |
| CV Line | 68 | 67.3 |

The echocardiography findings of this study were shown in Table (2). The study found that about 55 of 101 patients (54.4%) have normal pulmonary arterial pressure, and 46 of 101 patients (45.69%) have pulmonary hypertension, 31 of them (30.7%) have mild-moderate PHT, and 15 of them (14.9%) of them have severe PHT. We found that 20 of 101 patients (19.8%) have RV dysfunction, and 80.9% of patients have no RV dysfunction.

**Table (2):** Echocardiographic findings in patients with hemodialysis.

| Echo findings (n=101) | Frequency distribution | |
|---|---|---|
| | Number | Percentage |
| Left ventricular (LV) dysfunction | | |
| Dysfunction | 51 | 50.5 |
| No LV dysfunction | 50 | 49.5 |
| Ejection fraction | | |
| EF< 50% | 51 | 50.5 |
| EF≥ 50% | 50 | 49.5 |
| Left atrium (LA) | | |
| Dilated | 28 | 27.7 |
| Not dilated | 73 | 72.3 |
| Right atrium (RA) | | |
| Dilated | 17 | 16.8 |
| Not dilated | 84 | 83.2 |
| Left ventricular hypertrophy (LVH) | | |
| Yes | 64 | 63.4 |

| | | |
|---|---|---|
| No | 37 | 36.6 |
| Pulmonary arterial hypertension<br>Normal<br>Mild-moderate<br>Severe | <br>55<br>31<br>15 | <br>54.4<br>30.7<br>14.9 |
| Right ventricle (RV) function<br>dysfunction<br>no dysfunction | <br>20<br>81 | <br>19.8<br>80.2 |

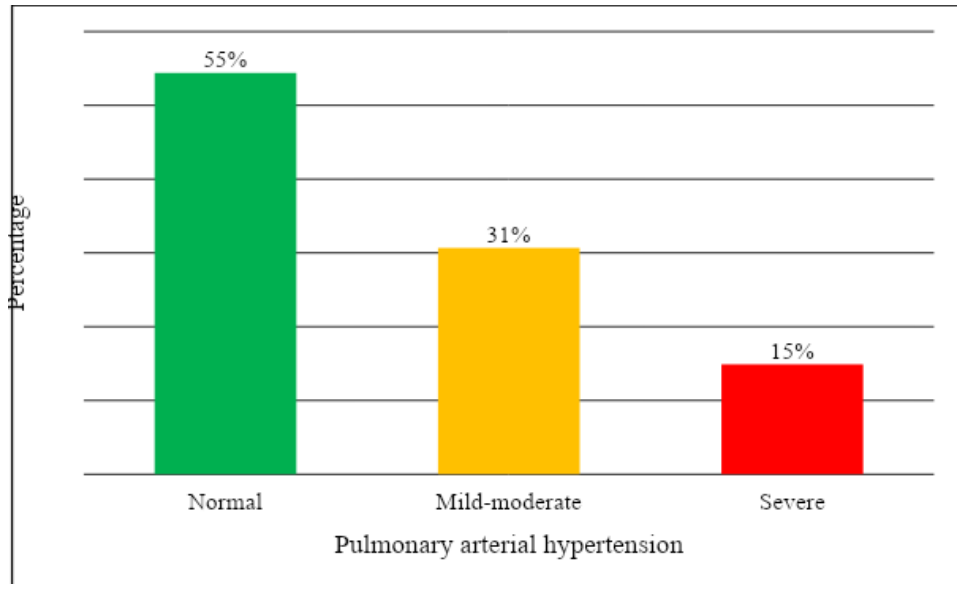


**Figure (1):** Prevalence of PHT in hemodialysis patients**.**

There are no significant differences in BMI, gender, vascular access, and causes of renal failure in patients with and without PHT. This study showed that the patients with mild-moderate PHT and those with severe PHT have LV dysfunction (25.49%) (25.49%), ejection fraction(EF%) <50% (25.49%) (25.49%),dilated LA(35.71%)(28.57%)and dilated RA (35.29%), (41.18%) respectively, with( 60%) of patients with RV dysfunction presented with severe PHT, while in those without PHT, LV dysfunction (49.02%),EF <50% (49.02%) ,LA(35.71%), RA (23.53%) and RV dysfunction (5.00%) .There is a significant association between RV dysfunction and severe PHT (p<0.001). Also there is a significant association between PHT and those with dilated LA, RA, LV dysfunction and low Ejection fraction (p=0.025),(p=0.002),(pj0.009),(p=0.009)re spectively . There is no significant association between PHT in patients with and without LVH Table (3).

**Table (3):** Comparisons of general characteristics and echo findings in patients with and without PHT.

| Characteristics (n=101) | Normal (n=55) | Mild-moderate (n=31) | Severe (n=15) | p-value |
|---|---|---|---|---|
| Age (yr.); mean (SD) | 48.4 (14.4) | 44.8 (16.2) | 55.7 (17.9) | 0.088[a] |
| BMI; Mean (SD) | 21.7 (3.2 | 23.5 (3.7 | 22.1 (3.4 | 0.161[a] |
| Gender; no (percentage)<br>Male<br>Female | <br>23 (48.94)<br>32 (59.26) | <br>16 (34.04)<br>15 (27.78) | <br>8 (17.02)<br>7 (12.96) | 0.579[b] |

| | | | | |
|---|---|---|---|---|
| Vascular access: no (%) | | | | 0.567[b] |
| AVF | 19 (57.58) | 8 (24.24) | 6 (18.18) | |
| CV line | 36 (52.94) | 23 (33.82) | 9 (13.24) | |
| Causes of RF; no(%) | | | | 0.517[b] |
| Diabetes mellitus | 11 (64.71) | 3 (17.65) | 3 (17.65) | |
| Glomerulonephritis | 2 (100) | 0 (0.0) | 0 (0.0) | |
| Hypertension | 6 (46.15) | 4 (30.77) | 3 (23.08) | |
| Other factors | 36 (52.17) | 24 (34.78) | 9 (13.04) | |
| LV; no (%) | | | | 0.009[b] |
| Dysfunction | 25 (49.02) | 13 (25.49) | 13 (25.49) | |
| No dysfunction | 30 (60.00) | 18 (36.00) | 2 (4.00) | |
| EF; no (%) | | | | 0.009[b] |
| < 50% | 25 (49.02) | 13 (25.49) | 13 (25.49) | |
| ≥ 50% | 30 (60.00) | 18 (36.00) | 2 (4.00) | |
| LA; no (%) | | | | 0.025[b] |
| Dilated | 10 (35.71) | 10 (35.71) | 8 (28.57) | |
| Not dilated | 45 (61.64) | 21 (28.77) | 7 (9.59) | |
| R; no (%) | | | | 0.002[b] |
| Dilated | 4 (23.53) | 6 (35.29) | 7 (41.18) | |
| Not dilated | 51 (60.71) | 25 (29.76) | 8 (9.52) | |
| LVH; no (%) | | | | 0.265[b] |
| Yes | 38 (59.38) | 16 (25.00) | 10 (15.63) | |
| No | 17 (45.95) | 15 (40.54) | 5 (13.51) | |
| RV; no (%) | | | | <0.001[b] |
| dysfunction | 1 (5.00) | 7 (35.00) | 12 (60.00) | |
| No dysfunction | 54 (66.67) | 24 (29.63) | 3 (3.70) | |

without PHT

[a]ANOVA-One way and [b] Pearson Chi squared tests were performed for statistical analyses.

## Discussion

The present study found that the prevalence of PHT among patients on HD was (45.6%). This finding is close to the results of Manuti study[14] which reported that the prevalence of PHT among chronic renal failure patients on regular HD was (42%) and the prevalence of PHT among chronic renal failure patients in pre dialysis stage was (24%). This study findings regarding the PHT in patients on HD are also close to results of Emara et al[15] study which reported PHT prevalence of (41.5%) among ESRD patients on HD. However, this study prevalence of PHT is lower than results of Hayati et al[16] cross-sectional study on 69 patients on HD which found that the prevalence of PHT was (62.3%)On the other hand, the reported prevalence of PHT in this study is higher than results of Zhang et al[17] study which showed PHT prevalence of (34.6%) among ESRD patients on HD. Globally, prevalence of PHT in patients on HD is ranging between 27%-58%[18-20]. In current study, 14.9% of patients on HD had severe PHT. This finding is close to results of Allawi et al[21] study which reported prevalence of severe PHT among patients on HD as (16.7%).Many literatures reported that severe PHT was found among 7%-29% of patients on HD[22-25]. The prevalence of RV dysfunction among patients on HD in the current study was (19.8%), This prevalence is close to results of Lee et al[26] study which found that 17.9% of patients on HD had RV dysfunction. However, this study prevalence of RV dysfunction is lower than the prevalence reported by Paneni et al[27] study of (71.3%). The present study showed a significant association between patients with left ventricular dysfunction and PHT (p=0.009). This finding is similar to results of Reque et al[28] prospective

study. This study found a significant association between patients with lower ejection fraction and PHT (p=0.009). This finding coincides with results of Zhao et al[29] study. The current study showed a significant association between patients with dilated left atrium and severe PHT (p=0.025). Paoletti et al[30] study stated that the LA dilation is considered as a significant predictor for adverse cardiovascularco-morbidities and mortality. The current study also showed a significant association between patients with dilated RA and severe PHT (p=0.002). This finding is consistent with results of Querejeta Roca et al[31] study. The interesting finding in this study was the highly significant association between RV dysfunction and severe PHT (p<0.001). This finding is in agreement with results of many literatures such as Al-Taii et al [32] study in Iraq and Zhao et al[29] cross study. Differences in PHT and RV dysfunction prevalence for patients on HD between different countries or various studies might be attributed to discrepancy in etiology of renal dysfunction, cardiovascular diseases and risk factors burden, age of patients and health infrastructure, and way of methods they use for assessment.

## Conclusion

The prevalence of PHT among patients on HD in Kurdistan region-Iraq is within Iraqi and international ranges studies, while the prevalence of right sided heart failure is low among HD patients. Current study recommended regular echocardiography monitoring of patients on HD with avoidance of cardiovascular complications. Limitations of this study, we evaluated the PHT by echocardiography, which is not superior to the right side cardiac catheterization in diagnosis of PHT.

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## Conflicts of interest

There were no conflicts of interest.

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