Abstract
Pulmonary hypertension (PHT) is a serious cardiac complication and highly prevalent in end-stage renal disease (ESRD). The aim of this study is to evaluate the PHT in ESRD and its relation with left and right side echocardiographic cardiac indices. Fifty patients with ESRD were included in the study. Echocardiography was used to evaluate systolic pulmonary artery pressure (sPAP), Tricuspid annular plane systolic excursion (TAPSE), cardiac output (CO), left ventricular mass (LVM). Cardiac index (CI) and left ventricular mass index (LVMI) were obtained by dividing CO and LVM on body surface area (BSA). The results are: Percentage of PHT in ESRD is about 50%. Percentage of abnormal LVM, LVMI, and TAPSE are: 76% (167-498 g), 78.9% (109-287 g/m²), and 18.4% (1.1-1.8 cm) respectively. Correlation study between PHT and TAPSE showed statistically significant negative correlation (r = -0.38, p < 0.05). Correlation studies of PHT with LVM and LVMI were weak correlation and statistically non-significant, but technically showed a positive correlation (r = 0.109, 0.094) respectively. The conclusion: pulmonary hypertension is extraordinary common among hemodialysis patients and volume overload have played an important role in the mechanism of pulmonary hypertension in end-stage renal disease.

Keywords: PHT, ESRD, LVM, LVMI.

الخلاصة
ارتفاع ضغط الشريان الرئوي من المضاعفات القلبية الخطيرة وكثر الحدوث في المرحلة النهائية للمرض الكلوي. تهدف الدراسة إلى تقييم ارتفاع ضغط الدم الرئوي لدى المرضى في المرحلة النهائية للمرض الكلوي وعلاقته مع مؤشرات القلب للجهتين اليمنى واليسرى بواسطة تخطيط صدى القلب. في هذه الدراسة أدرج خمسون مريض من الذين يعانون من المرض الكلوي في المرحلة الأخيرة في الدراسة. تم استخدام تخطيط صدى القلب لتقدير ضغط الشريان الرئوي الانقباضي (sPAP), شريان الرئوي الانقباضي (TAPSE), شريان الرئوي الانقباضي (CO), شريان الرئوي الانقباضي (CI), كتس الطبيين الأيسر (LVM), كتلة الطبيين الأيسر (LVMI). تم الحصول على مؤشر الطبيين الأيسر (CI), كتلته الطبيين الأيسر (LVM), كتلة الطبيين الأيسر (LVMI) بقسمة قيمتهم على مساحة سطح الجسم (BSA). وكانت النتائج: نسبة ارتفاع ضغط الدم الرئوي في المرضى في المرحلة النهائية حوالي 50%. نسبة المئوية لكتلة الطبيين الأيسر مؤشر كتلة وكتلة الطبيين الأيسر. وكتلة الطبيين الأيسر هي: 76% (167-498 غم), 78.9% (109-287 غم/م²), و 18.4% (1.1-1.8 سم) على التوالي. وأظهرت الدراسة ارتباط ضغط الدم الرئوي و TAPSE علاقة سلبية ذات دالة إحصائية (r = -0.38 (p < 0.05). و pokzrot الدراسة ارتباط بين ارتفاع ضغط الدم الرئوي وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع كتلة الطبيين الأيسر وLVMI ارتفاع ضغط الدم الرئوي مع Kt/V في آلية ارتفاع ضغط الدم الرئوي في المرحلة النهائية للمرض الكلوي.

الكلمات المفتاحية: ارتفاع ضغط الدم للشريان الرئوي, المرحلة النهائية للمرض الكلوي, كتلة الطبيين الأيسر, مؤشر كتلة الطبيين الأيسر.
Introduction

PHT is defined as mean pulmonary artery pressure (mPAP) of at least 25 mm Hg at rest [1]. PHT also is defined as systolic pulmonary artery pressure (sPAP) >40 mmHg [1]. PHT is a serious cardiac complication among patients with end-stage renal disease (ESRD) [2]. The pathogenesis of PHT in this population remains poorly understood. In a more recent study of patients receiving hemodialysis (HD) treatment, PHT was the strongest predictor of mortality [3]. For that reason evaluation of PHT is mandatory in routine assessment of uremic patients. TAPSE: Tricuspid annular plane systolic excursion is a validated parameter of global right ventricular (RV) function [4]. It describes apex-to-base shortening [5,6]. Echocardiographic assessment of (RV) function remains difficult because of its complex geometry. Standard echocardiographic parameters of RV function, such as ejection fraction (RVEF), are excellent theoretical entities but, due to suboptimal RV endocardial definition, may have limited value in current clinical practice [7]. TAPSE correlates closely with the RVEF [8], and has been found to be both highly specific and easy to measure [9]. Low TAPSE means reduced cranio-caudal excursion of tricuspid annulus, sign both of reduced ejection fraction and reduced distensibility of right ventricle [10]. Nephrologists usually need to have notion of a large number of parameters in the management of ESRD. Despite their efforts, they rarely have confidence with right heart functionality, even if this datum appears often crucial to hemodialysis vascular access policy and volumes management.

LVM, LVMI: Increase LVM defines left ventricular hypertrophy. Both M-mode and two-dimensional imaging can be employed to calculate left ventricular mass. M-mode imaging allows better endocardial border definition as it has greater resolution due to higher frame-rate, as long as adequate ultrasound beam positioning is ensured and ventricle shape approaches normality [11]. Normal range of LVM and LVMI are 67-162 g, and 43-95 g/m² respectively.

Aim is to evaluate the PHT in ESRD and its relation with left and right side echocardiographic cardiac indices.

Methods

This cross sectional study was performed at Shaheed AL-Mihrab for cardiac catheterization at Babylon province, from December 2015 to March, 2016. 50 patients were included in this study, with ESRD on hemodialysis, (21 female and 29 male) with mean age (53±12) year. Exclusion criteria include: any patient with possible cause of PHT other than ESRD, like patients with underlying lung disease, congenital heart disease, and others. Weight and height were taken for them to calculate the BSA according to Mosteller formula (BSA (m²)=√weight(Kg)*height (cm)/3600). Two-dimensional, M-mode, and Doppler echocardiography exams were performed on all of the patients by one experienced echocardiologist. Vivid-E9 imaging system (USA), equipped with a 3.2 MHz transducer, was used. Multiple views using different acoustic windows were obtained to measure the most optimal tricuspid regurgitation (TR) jet signal using continuous wave (CW) Doppler. sPAP was estimated based on the modified Bernoulli equation as follows [12]: 4 V² (V = peak velocity of TR in meters per second, obtained using the CW Doppler) was added to the estimated right atrial pressure (RAP). The RAP was estimated based on the dimensions of the inferior vena cava (IVC) during inspiration, figure 1. The RAP was estimated to be 5 mmHg if the IVC size was less than 2.0 cm and collapsed by 50% during inspiration, 10 mmHg if the IVC was less than 2.0 cm and did not collapse by 50%, 15 mmHg if the IVC was greater than or equal to 2.0 cm and collapsed more than 50%, and 20 mmHg if the IVC was greater than or equal to 2.0 cm and did not collapse by 50% [1].

By M-Mode of left parasternal long axis view measurement of stroke volume, according to Teichholz formula through the measurement of left ventricular internal dimension in diastole (LVIDd) and systole.
(LVIDs). By the same view measurement of the LVM by measuring LVIDd, PWTd, and IVSd: [13](figure 2)

\[ \text{LVmass} = 0.8 \times (1.04 \times ([\text{LVIDD} + \text{PWTD} + \text{IVSTD}]^3 - [\text{LVIDD}]^3)) + 0.6 \ g. \]

Where: LVIDD = Left Ventricular Internal Diameter in Diastole
PWTD = Posterior Wall Thickness in Diastole
IVSTD = Interventricular Septum Thickness in Diastole

LVMI: is obtained by dividing LVM on BSA .

TAPSE is assessed with M-mode in an apical four-chamber view, placing the M-mode cursor on the lateral tricuspid annulus. Maximum plane systolic excursion of the lateral annulus is measured. Figure 3.

Echocardiographic evaluation of diastolic function has been traditionally performed by measurement of transmitral flow parameters including the early (E) and late (A) diastolic filling velocities, the E/A ratio, and the E deceleration time (DT) from an apical four chamber view with conventional pulsed wave Doppler [14]. During echocardiographic assessment of the patients some cases were reported with mitral regurgitation, figure 4.

Figure 1: A.M-Mode and B.2D-Echocardiogram showing the inferior vena cava for assessment of right atrial pressure.
**Figure 2:** M-Mode echocardiogram in parasternal long axis view for measurement of SV, EF, LVM and LVMI.

**Figure 3:** M-Mode echocardiogram in an apical four-chamber view, placing the M-mode cursor on the lateral tricuspid annulus for measurement of TAPSE.

**Figure 4:** Apical echocardiographic view showing moderate to severe eccentric mitral regurgitation.
**Statistical Analysis**
Descriptive statistics (the mean values, standard deviations, and percentages) were used to describe the quantitative study variables. Pearson Correlation study was used to assess the correlation between parameters measured in the study. P value <0.05 was considered statistically significant.

**Results**
Echocardiographic parameters in this study were expressed as (mean ±SD ) and as a range in table-1.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (L/min)</td>
<td>7.65±2.989</td>
<td>3.53-11.76</td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>4.92±2.03</td>
<td>2.6-4.2</td>
</tr>
<tr>
<td>Left ventricular mass (g)</td>
<td>256.41±88.105</td>
<td>122-430</td>
</tr>
<tr>
<td>Left ventricular mass index (g/m²)</td>
<td>155.93±57.02</td>
<td>50-287</td>
</tr>
<tr>
<td>Pulmonary hypertension (mmHg)</td>
<td>42.37±16.6</td>
<td>41-75</td>
</tr>
<tr>
<td>TAPSE (cm)</td>
<td>2.27±0.47</td>
<td>1.1-2.86</td>
</tr>
<tr>
<td>Relative wall thickness (rWT)</td>
<td>0.47±0.103</td>
<td>0.3-0.69</td>
</tr>
</tbody>
</table>

Percentage of PHT is about 50%. 78.9% (109-287g/m²), and 18.4% (1.1-1.8 cm) respectively. Figure-5.

![Echocardiographic parameters in this study include:](image)

**Figure 5**: Percentage of abnormal values of Pulmonary pressure, LVM, LVMI, and TAPSE in ESRD patients

Correlation study between PHT and TAPSE showed statistically significant negative correlation (r = -0.38, p < 0.05), figure 6. Correlation studies of PHT with LVM and LVMI were weak correlation and statistically nonsignificant, but technically showed a positive correlation (r = 0.109, 0.094) respectively, figure 7, 8. Other findings during the study: All patients were with diastolic dysfunction ranging between grade I and II, and 26.3% of the patients were with mitral regurgitation.
**Figure 6:** Correlation between Tricuspid annular plane systolic excursion (TAPSE) and pulmonary hypertension (PHT) (P<0.05)

**Figure 7:** Correlation between pulmonary hypertension (PHT) and left ventricular mass (LVM)

**Figure 8:** Correlation between pulmonary hypertension and left ventricular mass index (LVMI)
Discussion
The present study demonstrates that PHT is relatively common in the patients receiving hemodialysis and this goes with recent observational studies that reported a high prevalence of PHT in ESRD, particularly among HD patients [15-17] and an association with adverse outcomes [3]. Arteriovenous fistula are considered the gold standard for HD access [18]. They result in increased venous return with a concomitant increase in cardiac output, and this may explain the high level of CO and CI in this study. Cases of 'high output cardiac failure' as a result of high AVF flow are not uncommon and often necessitate fistula ligation or reduction [19]. This was one of the first mechanisms proposed as a cause for PHT in patients receiving HD. Both ESRD and long-term hemodialysis via arteriovenous access may be involved in the pathogenesis of PHT by affecting pulmonary vascular resistance and cardiac output[1]. Bolignano and his colleagues in 2013 demonstrated that Pulmonary hypertension in patients with chronic kidney disease (CKD) may be induced and/or aggravated by left ventricular disorders and many risk factors typical of CKD like volume overload and an arteriovenous fistula [20]. Yigla et al.[21] showed that the only significant difference between patients who developed PHT and those who did not was higher cardiac output, suggesting that in the setting of abnormal cardiac function, an increase in flow may result in an increase in mPAP.

High cardiac output in this study could explain the concentric LVH that demonstrated by high LVM and LVMI with rPWT which reflects concentric hypertrophy. Presence of 26.3% Mitral valve incompetence in HD patients is usually functional and reflects the fluid status of the patient and this is in accordance with Rosenberger et al in 2005[22]. This study demonstrate low percentage of abnormal TAPSE readings in the existence of PHT. So the echocardiogram in this study strongly points toward a left heart origin of PHT as there is marked LVH (demonstrated by high LVM and LVMI), LV diastolic dysfunction. RV function is preserved as evidenced by normal TAPSE (as TAPSE is clinically useful echocardiographic measure of global RV function [23,24]. These findings are in agreement with Raina in 2013 [25]. Beigi and Malhotra and their colleagues, in 2009 and 2012 respectively, stated that an inappropriately high cardiac output with a noncompliant, hypertrophied left heart will lead to left heart congestion, with PHT being an inevitable consequence [26,27].

This study can formulate hypotheses, about the importance of early detection of LVH due to volume overload and the presence of PHT in patients with ESRD to plan a hemodialysis arterio-venous fistula.

Conclusion
Pulmonary hypertension is extraordinary common among hemodialysis patients and volume overload have played an important role in the mechanism of pulmonary hypertension in end stage renal disease on hemodialysis. We suggest to all cardiologists and to nephrologists concerned to the execution of echocardiography to detect systematically: PHT, TAPSE, LVM, LVMI, CO and CI in all patients, particularly when they go planning the packaging of a vascular access for hemodialysis.

References
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