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Prevalence of Right Ventricular Systolic Dysfunction among Patientswith End-Stage Renal Disease on Regular Hemodialysis

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Abstract

Aim: There is a growing controversy regarding the frequency of right ventricular dysfunction among end-stage renal disease on regular hemodialysis. The present study aimed to assess the frequency of right ventricular dysfunction among patients with end-stage renal disease on regular hemodialysis.

Methods: The present study was a cross-sectional study conducted during the period from September 2019 to February 2020 at the Dialysis Unit, Internal Medicine department, Aswan University Hospital. Patients who were diagnosed with end-stage renal disease and scheduled for maintenance hemodialysis were recruited. A non-probability sampling technique was employed to recruit eligible patients.

Results: Out of the enrolled 100 patients, 44% had right ventricular dysfunction based on right ventricular global longitudinal strain. Regarding echocardiographic parameters, 17.9% of patients with normal right ventricular function had high pulmonary artery systolic pressure versus 31.8% of patients with abnormal right ventricular function, 19.6% of patients with normal right ventricular function had dilated left atrium versus 34.1% of patients with abnormal right ventricular function and left ventricle ejection fraction in patients with normal right ventricular function is higher than patients with abnormal right ventricular function (66.57 ± 8.4% versus 58.16 ± 10.8%, $P < 0.001$).

Conclusion: Subclinical right ventricular dysfunction affects a considerable proportion of end-stage renal disease patients and may have significant implications on the disease course. Nevertheless, larger studies are still needed to confirm these findings.

Keywords: End-stage renal disease; Hemodialysis; Right ventricular dysfunction.

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I. Introduction:

Chronic kidney disease (CKD) is defined as a debilitating disorder with cardinal feature of progressive deterioration in the anatomical structure and/or function of the kidney persisting for more than three months (1). CKD is a global health problem with an estimated prevalence of 7–12%, worldwide (2). According to pervious epidemiological studies, higher prevalence was observed in developing countries with an estimated figures ranged between 10% and 16% (3). Moreover, CKD may lead to wide range of complications including cardiovascular diseases, metabolic acidosis, and hematological complications (4). End-stage renal disease (ESRD) is the final stage of CKD that is characterized by irreversible kidney damage and lifelong need for renal replacement therapy (5). The incidence of ESRD has dramatically increased over the past few decades owing to the increased longevity of the population and the epidemic of diabetes (6).

As a consequence of CKD, patients with ESRD are prone to excessive risk of various morbidities, such as cardiovascular morbidities, bone mineral disturbance, metabolic abnormalities, and anemia (7). Besides, ESRD is a leading cause of mortality worldwide (8). Furthermore, it was reported that ESRD was associated with reduced quality of life and depressive disorders (9). As well, ERSD endured an economical burden, especially for low and Middle-income countries; patients with ERSD required frequent hospitalization and periodic hemodialysis with increased health care expenditure (10).

It was found that cardiac complications are frequent among patients with CKD. According to cumulative evidence, about one-fifth of CKD patients developed left ventricular (LV) heart failure during the course of their disease (11). This figure increased dramatically as patients reached the ESRD phase (12). As the exact pathogenic mechanisms underlying LV function deterioration in CKD patients was not fully explained, various mechanisms were proposed as possible contributors. Firstly, the longstanding hypertension and excessive water retention that can lead to excessive preload in CKD patients (13). Secondly, patients with CKD exhibits variable degree of cardiomyopathies including ventricular hypertrophy and fibrosis (12).

Thirdly, the presence of significant arterial stiffness, ischemic changes, excessive inflammatory mediators, anemia, and high shunt output in patients with CKD and ESRD can be considered as another contributing factors to the development of heart failure (12,14).

Recently, a growing body of evidence highlighted the significant increase in the risk of right ventricular (RV) dysfunction in patients with ESRD (15). The presence of RV dysfunction can have many negative effects on ESRD patients; for example, impaired RV function may lead to further compromise in LV function. Also, RV dysfunction is associated with increased risk of arrythmia, cardiac shock, and hence mortality (16). Thus, it is important to understand the prevalence and pathogenesis of RV dysfunction in ESRD patients.

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Although patients undergoing chronic dialysis exhibit an increased prevalence of pulmonary hypertension during treatment, data on the development of right ventricular dysfunction (RVD) are lacking. Moreover, in patients with pulmonary hypertension, survival has been related to cardiac function rather than pulmonary pressure values (17). Importantly, RVD may also affect left ventricular filling via interventricular interaction (18).Nonetheless, there is a growing controversy regarding the frequency of RV dysfunction among ESRD patients on regular hemodialysis. The present study aimed to assess the frequency of RV dysfunction among patients with ESRD on regular hemodialysis.

II. Materials and Methods:

i. Study Design, Setting, and Patients:

The present study was a cross-sectional study conducted in the time from September 2021 to February 2022 at Internal Medicine department, Aswan University Hospital. Patients diagnosed with ESRD and scheduled for maintenance hemodialysis were included. On the other hand, those with acute renal failure were excluded. A non-probability sampling technique was employed to recruit eligible patients.

ii. Sample size calculation

Sample size calculation was carried out using G*Power 3 software (Faul et al., 2007). A minimum calculated sample of 82 patients will be needed to detect an effect size of 0.4 in the frequency of RV failure among CKD patients, with an error probability of 0.05 and 95% power.

iii. Data collection:

Data was collected from all patients included: demographic characteristics, duration since the start of hemodialysis, risk factors for ESRD, clinical examination findings, laboratory investigations findings, and echocardiography findings. Images were obtained with left lateral decubitus using Philips Healthcare (Philips xMATRIX iE 33). Data acquisition was conducted in parasternal and apical views using X5-1 transducer. Standard M-mode, 2D, and Doppler blood flow measurements were performed, and three consecutive beats were saved in cineloop format in RV focused apical 4-chamber view. Pulmonary artery systolic pressure (PASP) was estimated from the peak continuous-wave Doppler velocity of tricuspid valve regurgitation plus the estimated RA pressure. No patient had 2D or Doppler evidence of pulmonary valve stenosis or RV outflow tract obstruction. RV function was assessed using an off-axis apical 4-chamber view for better visualization of RV. Tricuspid annular plane systolic excursion (TAPSE) was measured by placing an M-mode cursor through the lateral tricuspid valve annulus in the apical 4-chamber view and measuring the total systolic excursion distance of the tricuspid annulus. Peak systolic velocity (PSV) of the lateral tricuspid valve annulus was measured by tissue Doppler imaging.

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Using speckle-tracking echocardiography (STE) analysis, peak longitudinal systolic strain was measured from an RV-focused apical 4-chamber view with the RV positioned centrally in the imaging sector. The measurements were performed online using dedicated software (Automated Functional Imaging; GE Healthcare). A region of interest was traced by placing points along the RV endocardial border and adjusting the thickness of the myocardium accordingly.

The Automated Functional Imaging software then uses a tracking algorithm to trace endocardial and epicardial contours throughout the cardiac cycle, which can be manually adjusted to the RV myocardium to ensure adequate tracking. The RV free wall is automatically divided into basal, middle, and apical segments. Peak longitudinal systolic strain was obtained for each segment from curves and averaged for a mean RV free-wall strain value.

iv. Statistical Analysis:

Data entry, processing, and analysis was carried out using Microsoft Excel 2007 (Microsoft Corporation, NY, and the USA) and IBM-SPSS-22 (Statistical Package for the Social Science; IBM-SPSS Inc., Chicago, IL, USA). Quantitative data was described in terms of mean ± standard deviation (SD)/median (range), while qualitative data were expressed as frequencies and percentages. Comparisons between quantitative variables were conducted using unpaired Student's t-test for parametric data or Mann-Whitney Rank Sum test for non-parametric data. Chi-square test was performed for categorical variables. Logistic regression analysis was calculated to investigate the significant factors influencing LV failure (Odds Ratio -OR-, 95% confidence interval -95% CI- p-value). A probability value (p-value) less than 0.05 was considered statistically significant.

v. Ethical Consideration

Hereby, the authors confirmed that the current study abided with guidelines stated by the Declaration of Helsinki. The study protocol obtained approval from the local ethics and research committee of Aswan university hospital, Awritten informed consent was obtained from all eligible patient prior to the onset of the study field work.

III. Results:

The current study enrolled 120 patients who had ESRD on regular hemodialysis in the Hemodialysis Unit of Aswan University Hospital. Twenty patients were excluded from the study because of refusal either to participate or to undergo TTE. Finally, 100 patients participated in this study (**Fig. 1**).

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Socio-demographic and clinical characteristics of the studied cohort were shown in **Table 1.** The mean age of the patients was 47.9 ± 13.9 years, male/female ratio was approximately 1:1, about three-quarters was married, about two-thirds was unemployed and about one-third was smokers. Moreover, the majority of patients had HTN (75%), 15% had DM, 10% had IHD and 7% had Chest Diseases. Also, the mean duration of hemodialysis was 4.4 ± 3.5 years.

Table 2 showed the main laboratory findings among the studied patients. The mean hemoglobin levels was 10.4 ± 1.5 gm/dl, the mean platelet count was 213.5 ± 99.8 $*10^3$/cubic mm and the mean random blood glucose was 127.9 ± 71.5 mg/dl. Furthermore, the mean urea level was 131.5 ± 35.5 mg/dl, the mean creatinine level was 9.2 ± 2.8 mg/dl, the mean sodium level was 136.9 ± 10.9 mEq/l, the mean potassium level was 5.6 ± 0.9 mEq/l, the mean calcium level was 8.4 ± 0.9 mg/dl, and the mean uric acid level was 6.9 ± 1.7 mg/dl.

Echocardiographic parameters of the studied patients were illustrated in **Tables 3**. The mean TAPSE for the patients was 2.4 ± 0.5 cm with only 3% abnormal RVF, the mean S' was 14.2 ± 3.3 cm/sec with 9% abnormal RVF and the mean RV-GLS was -20.7 ± 5.8% with 44% abnormal RVF. Of the studied patients, about one-quarter (24%) had high PASP (more than 35 mm Hg) and (26%) dilated left atrium (more than 4 cm). Also, 44% had tricuspid regurgitation and 38% had mitral regurgitation. Further, the mean LV ejection fraction of the studied patients was 62.9 ± 10.4% and about two-thirds (65%) of these patients had LV diastolic dysfunction. Based on RV-GLS, about half (44%) of the studied patients had RV dysfunction.

Tables 4 & Figure 3 presented the differences between the two groups (normal RV function vs. abnormal RV function) regarding socio-demographic, clinical, laboratory and echocardiographic determinants. There was no statistically significant difference between both groups regarding socio-demographic, clinical characteristics, and laboratory parameters. Regarding the echocardiographic parameters, 17.9% of patients with normal RV function had high PASP versus 31.8% of patients with abnormal RV function (P value 0.048). Likewise, significantly higher proportion of patients with abnormal RV function (about one-third -34%%-) had dilated left atrium compared with one-fifth (19.6%) in patients with normal RV function (P value=0.044). Also, statistically significant higher mean LV ejection fraction was reported in patients with normal RV function vs. those with abnormal RV function (66.6 ± 8.4% versus 58.2 ± 10.8%, P < 0.001).

Table 5 displayed the predictors of LVD among the studied cohort. In the final multivariable model, after adjusting for age and sex, there were five predictors: DM history, High PASP, Dilated LA, MR and LVEF%. In other words, the likelihood of having RVD was associated with positive DM history (AOR=1.8, 95% CI: 1.1–3.1, p=0.032), high PASP (AOR=2.1, 95% CI: 1.1–4.1, p=0.041), Dilated LA (AOR=2.5, 95% CI: 1.1–4.9, p=0.045), MR (AOR=1.5, 95% CI: 1.1–2.7, p=0.044) and with decrease in the LVEF% (AOR=0.91, 95% CI: 0.86–0.96, p=0.001).

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IV. Discussion:

Right ventricular myocardial functions have been insufficiently studied in patients with ESRD. In the present study, it was found that 44% of the ESRD patients had RV dysfunction based on RV-GLS. About one-third of these patients had high PASP and dilated LA. The association analysis demonstrated that patients with RV dysfunction had lower LV ejection fraction than patients without RV dysfunction. This study hypothesized that our findings stem from a combination of different factors that are peculiar to patients with ESRD. Firstly, the current body of evidence showed that regular dialysis does not effectively correct uremia and metabolic abnormalities in ESRD patients, which may lead to toxic effects RV microstructure and function (19). In addition, the long-standing hypertension in ESRD significantly impaired the strain function of the patients.

The current results were in line with Paneni et al. (20), who demonstrated high incidence of RV dysfunction in ESRD patients. Similar findings were reported by Peng et al. (15), in a more recent report. In a study by Momtaz et al. (21), patients on regular hemodialysis exhibited higher incidence of RV dysfunction than normal population. In an Egyptian study in 2016, patients on regular hemodialysis were found to exhibit higher incidence of RV dysfunction than newly-diagnosed patients with preserved systolic function (22). In our study, we found that TAPSE of the studied patients was 2.35 ± 0.5 cm. This is discordant with **Najafian J et al**. (23) who studied right ventricular function and pulmonary artery pressure before and shortly after hemodialysis in patients with end-stage renal disease. They found that TAPSE of the patients after hemodialysis was 1.81 ± 0.43 cm. This can be explained by the difference in the time of echocardiographic examination of the patients as they examined the patients 30 minutes after termination of the hemodialysis session while we examined the patients 1 hour after termination of the hemodialysis session**.**

In our study, we found that RV GLS of the patients was -20.71% ± 5.8. This is consistent with **Tamulėnaitė E et al**.(24) who studied Changes of Left and Right Ventricle Mechanics and Function in Patients with End-Stage Renal Disease Undergoing Haemodialysis. They found that RV GLS of the patients was -22.96% ± 3.04

Moreover, in this study, patients were further classified into two groups based on RV GLS: (group I: patients with normal RVF (n=56) and group II: patients with RVD (n=44) (Normal RV GLS </= -20%). There were statistically insignificant differences between both groups regarding basic socio-economic, clinical characteristics or laboratory parameters. On the other hand, it was found that patients with RVD had high PASP, dilated LA and lower LVEF than patients with normal RVF. So, PASP, LA diameter and LVEF were identified as major contributors to RVF measured as RV-GLS. These results were consistent with Lopez-Quijano et al (25). who found that LVEF, LV mass index and myocardial relaxation velocity were considered major contributors to RV systolic function.

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V. Conclusion:

In conclusion, subclinical RV dysfunction affects a considerable proportion of ESRD patients and may have significant implications on the disease course among the affected patients. The current study also highlighted that STE is a useful tool for detection of subclinical RV dysfunction in patients with ESRD on regular hemodialysis when other parameters are normal. So, 2D-STE should be a routine for assessment of the RV function in patients with ESRD on regular hemodialysis. Nevertheless, larger studies are still needed to confirm our findings.

DISCLOSURE:

There is no conflict of interest in this work.

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Table 1. Baseline Socio-Demographic Characteristics of Study group

Parameter		**n = 100**
Age in years	• **Mean ± SD** • **Median (Range)**	47.87 ± 13.9 46.5 (23 - 82)
Sex	• **Female** • **Male**	54 (54%) 46 (46%)
Occupation	• **Non-working** • **Working**	67 (67%) 33 (33%)
Marital Status	• **Married** • **Unmarried**	73 (73%) 27 (27%)
Smoking Status	• **Smoker** • **Non-smoker**	29 (29%) 71 (71%)
DM	• **Yes**	15 (15%)
HTN	• **Yes**	75 (75%)
IHD	• **Yes**	10 (10%)
Chest Disease	• **Yes**	7 (7%)
Dialysis Duration/years	• **Mean ± SD** • **Median (Range)**	4.42 ± 3.5 4 (0.1 - 19)

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Table 2. Laboratory parameters of the studied Cohort

Parameter		n = 100
RBCs (mc/L)	• **Mean ± SD** • **Median (Range)**	3.66 ± 0.5 3.7 (1.9 – 4.7)
Hemoglobin (gm/dl)	• **Mean ± SD** • **Median (Range)**	10.37 ± 1.5 10.4 (6.0 – 13.6)
WBCs (mc/L)	• **Mean ± SD** • **Median (Range)**	6.76 ± 2.5 6.3 (2.0 – 16.1)
Platelet*10^3	• **Mean ± SD** • **Median (Range)**	213.51 ± 99.8 206.5 (20 – 767)
RBG (mg/dl)	• **Mean ± SD** • **Median (Range)**	127.89 ± 71.5 110 (68 – 528)
Blood Urea (mg/dl)	• **Mean ± SD** • **Median (Range)**	131.50 ± 35.5 132 (25 – 217)
Serum Creatinine (mg/dl)	• **Mean ± SD** • **Median (Range)**	9.18 ± 2.8 8.8 (3 – 20)
Sodium (mEq/L)	• **Mean ± SD** • **Median (Range)**	136.86 ± 10.9 136 (128 – 150)
Potassium (mEq/L)	• **Mean ± SD** • **Median (Range)**	5.55 ± 0.9 5.8 (3.3 – 7.8)
Calcium (mEq/L)	• **Mean ± SD** • **Median (Range)**	8.40 ± 0.9 8.5 (6.0 – 10.5)
Uric Acid (mg/dl)	• **Mean ± SD** • **Median (Range)**	6.92 ± 1.7 7.0 (3.5 – 11.5)

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Table 3. Echocardiographic parameters of the studied group

Parameter		n = 100
TAPSE	• **Mean ± SD** • **Median (Range)**	2.35 ± 0.5 2.3 (0.8 – 3.9)
TAPSE Category	• **Abnormal RVF (< 1.5)**	3 (3%)
S'	• **Mean ± SD** • **Median (Range)**	14.21 ± 3.3 14 (7 – 24)
S' Category	• **Abnormal RVF (< 10)**	9 (9%)
RVGLS %	• **Mean ± SD** • **Median (Range)**	-20.71 ± 5.8 -20 (-43: -8)
RVGLS Category	• **Abnormal RVF (>-20%)**	44 (44%)
PASP	• **High**	24 (24%)
LA	• **Dilated**	26 (26%)
TR	• **Mild** • **Moderate** • **Severe**	24 (24%) 11 (11%) 9 (9%)
MR	• **Mild** • **Moderate** • **Severe**	13 (13%) 17 (17%) 8 (8%)
LV EF%	• **Mean ± SD** • **Median (Range)**	62.87 ± 10.4 64 (30 – 79)
LVDD	• **Grade I** • **Grade II** • **Grade III**	41 (41%) 14 (14%) 9 (9%)

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Table 4: Univariate Correlates of RVD among the studied Cohort

		Normal RVF (n=56)	Abnormal RVF (n=44)	P-value
Age/years	**Mean ± SD**	47.04 ± 13.5	48.93 ± 14.4	= 0.504*
Sex	**Female**	28 (50%)	26 (59.1%)	= 0.241**
	Male	28 (50%)	18 (40.9%)	
Occupation	**Non-working**	34 (60.7%)	33 (75%)	= 0.132**
	Working	22 (39.3%)	11 (25%)	
Marital Status	**Married**	41 (73.2%)	32 (72.7%)	= 0.567**
	Unmarried	15 (26.8%)	12 (27.3%)	
Smoking	**Non-smoker**	38 (67.9%)	33 (75%)	= 0.289**
	Smoker	18 (32.1%)	11 (25%)	
DM		7 (12.5%)	8 (18.2%)	= 0.304*
HTN		45 (80.4%)	30 (68.2%)	= 0.123*
IHD		7 (12.5%)	3 (6.8%)	= 0.123*
Chest Infection		4 (7.1%)	3 (6.8%)	= 0.633*
Dialysis Duration		4.85 ± 0.6	3.88 ± 0.4	= 0.149**
RBCs (mc/L)		3.65 ± 0.6	3.67 ± 0.5	= 0.809**
Hemoglobin (gm/dl)		10.32 ± 1.6	10.44 ± 1.3	= 0.691**
WBCs (mc/L)		6.67 ± 2.4	6.86 ± 2.6	= 0.709**
Platelet *10^3/L		210.71 ± 92.6	217.07 ± 99.3	= 0.754**
Blood Urea (mg/dl)		132.33 ± 38.5	130.45 ± 31.7	= 0.789**
S. Creatinine (mg/dl)		9.17 ± 2.1	9.19 ± 2.4	= 0.973**
Sodium (mEq/L)		136.75 ± 3.5	136.59 ± 3.4	= 0.814**
Potassium (mEq/L)		5.47 ± 0.9	5.64 ± 0.8	= 0.354**
Calcium (mEq/L)		8.50 ± 0.8	8.27 ± 0.9	= 0.208**
Uric Acid (mg/dl)		6.91 ± 1.7	6.93 ± 1.4	= 0.943**
High PASP		10 (17.9%)	14 (31.8%)	**= 0.048***

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TR	20 (35.7%)	18 (40.9%)	= 0.373*
Dilated LA	11 (19.6%)	15 (34.1%)	**= 0.044***
MR	22 (39.3%)	22 (50%)	= 0.193*
LVEF%	66.57 ± 8.4	58.16 ± 10.8	**< 0.001****
LVD	37 (66.1%)	27 (61.4%)	= 0.390*

Table 5: Predictors of RVD among Stroke Patients: Logistic Regression Model

Variable	Univariate		Multivariable	
	OR (95% CI)	**P-value**	**HR (95% CI)**	**P-value**
Age/years	1.010 (0.981–1.039)	= 0.496	1.012 (0.947–1.095)	= 0.621
Sex (Male)	0.692 (0.312–1.536)	= 0.366	1.241 (0.845–2.656)	= 0.215
Smoker	0.704 (0.294–1.702)	= 0.436		
History of HTN	0.524 (0.210–1.308)	= 0.166		
History of DM	1.556 (0.517–4.682)	= 0.232	1.812 (1.021–3.241)	**= 0.032**
PASP (High)	2.147 (1.012–3.456)	**= 0.024**	2.041 (1.036–4.006)	**= 0.041**
TR	1.545 (0.980–3.015)	= 0.161		
Dilated LA	2.116 (0.814–4.242)	= 0.105	2.508 (1.084–4.881)	**= 0.045**
MR	1.360 (1.083–2.018)	= 0.065	1.441 (1.015–2.642)	**= 0.044**
LV EF%	0.908 (0.861–0.956)	**< 0.001**	0.910 (0.862–0.960)	**= 0.001**
LVD	0.943 (0.615–1.446)	= 0.788		

OR =Odds Ratio; CI, Confidence Interval

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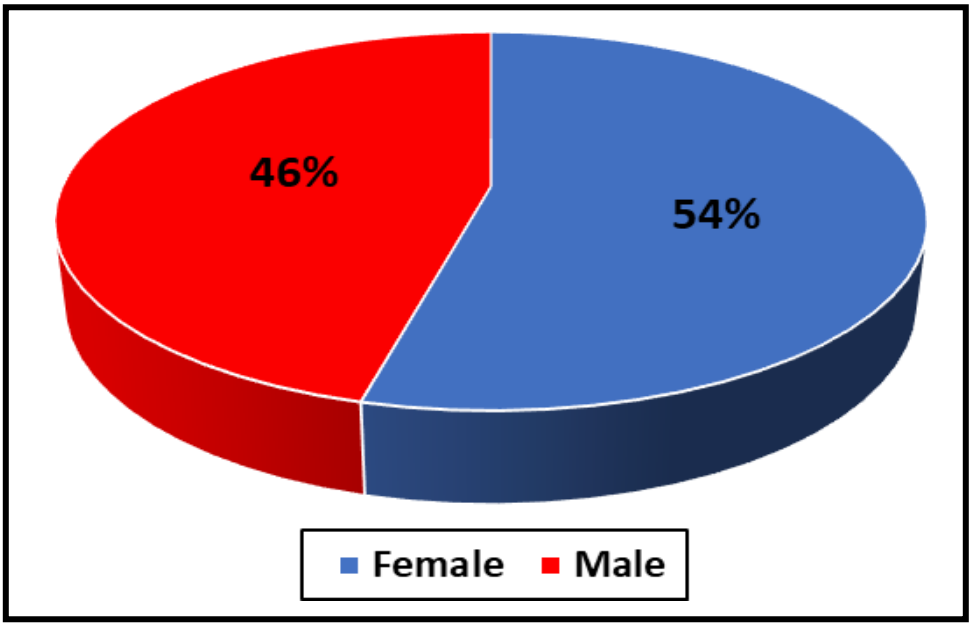

Fig. 1: Sex Distribution of the studied Cohort

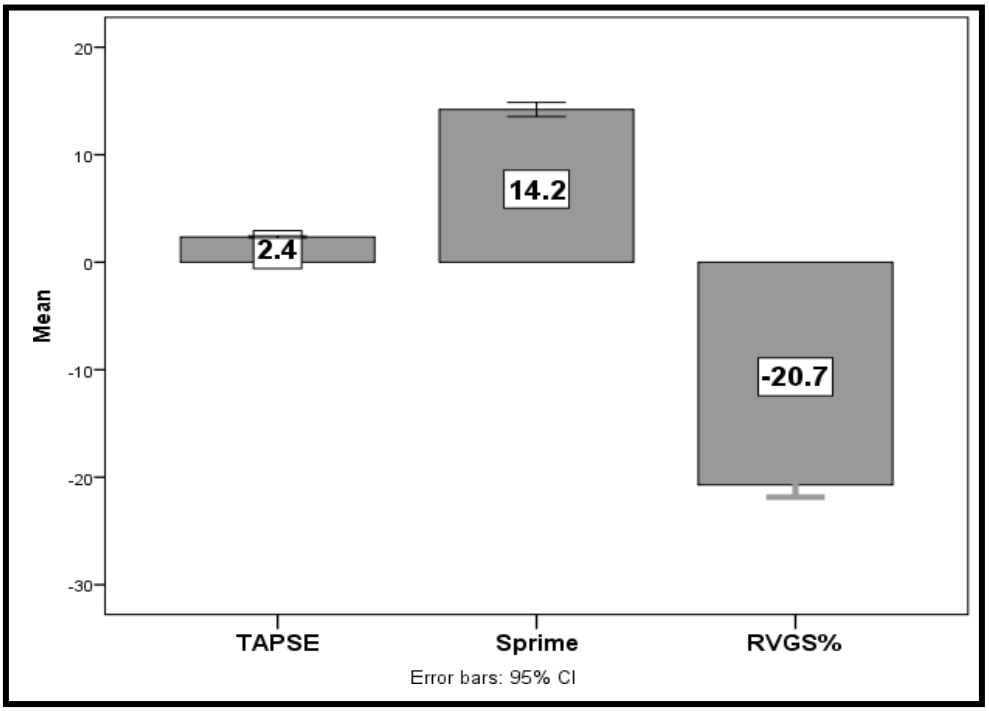

Fig. 2: Mean RVF Parameter Level of the Study group

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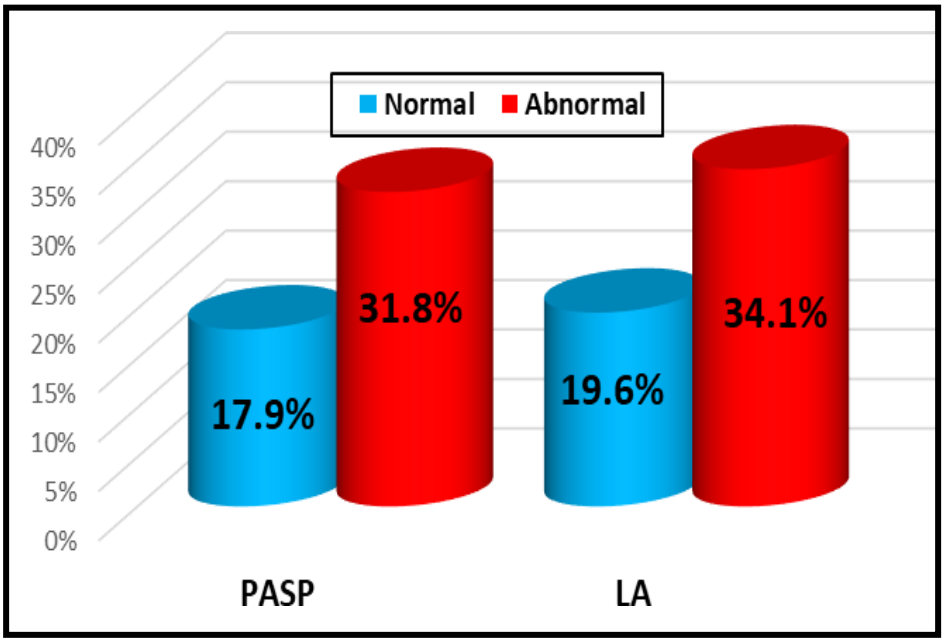

Fig. 3: PASP and LA Abnormality in Normal VS Abnormal RVF