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Determining The Prevalence of Right Ventricular Systolic Dysfunction in Diabetic and Non-Diabetic Patients Having Pulmonary Hypertension in Rehman Medical Institute, Peshawar

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Abstract

Background: Right ventricular (RV) dysfunction is a major determinant of prognosis in patients with pulmonary hypertension (PH). Diabetes mellitus (DM) is associated with structural and functional cardiac changes, which may exacerbate RV impairment in PH patients. However, the frequency and extent of RV dysfunction in diabetic versus non-diabetic PH patients remains underexplored.

Objective: To determine the frequency of right ventricular dysfunction in diabetic and non-diabetic patients with pulmonary hypertension.

Vol. 5 No. 1 (2026)

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Samad et al - 2026

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Methods: An observational cross-sectional study was conducted at the Cardiology Department of Rehman Medical Institute, Peshawar, over a period of three months. A total of 353 patients aged 20–65 years with PH were included using a convenient non-probability sampling technique. Patients with congenital heart disease or who were non-cooperative were excluded. Data were collected through self-administered questionnaires and analyzed using SPSS version 2022. RV dysfunction was assessed in terms of right ventricular hypertrophy (RVH), tricuspid regurgitation (TR), and pulmonary regurgitation (PR).

Results: Among 353 participants, 191 (54.1%) were diabetic and 162 (45.9%) were non-diabetic. Male patients comprised 63.46% and females 36.54% of the study population. RV dysfunction, including RVH and TR, was significantly more frequent in diabetic patients compared to non-diabetic patients ($p < 0.05$). Diabetic PH patients demonstrated higher prevalence of structural and functional RV impairment, highlighting the additive effect of diabetes on right ventricular pathology in PH.

Conclusion: Patients with diabetes and pre-existing pulmonary hypertension are more likely to develop right ventricular dysfunction compared to non-diabetic PH patients. Early recognition and monitoring of RV function in this population is critical to improve clinical outcomes.

INTRODUCTION

For many years in the field of cardiology, the function of the right ventricle was underestimated and neglected (1). The increasing identification of the critical role of the right ventricle in determining cardiac function and prognosis is now being recognized. The main function of the right ventricle is to receive deoxygenated blood from the right atrium and transport it to the lungs through pulmonary arteries for oxygenation. In certain

Vol. 5 No. 1 (2026)

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Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

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conditions, right ventricular function and mechanism deviate from normal under settings of either pressure or volume overload, leading to pulmonary hypertension (2). In pulmonary hypertension particularly, right ventricular function can be impaired and is closely related to survival (3). An accurate assessment of right ventricular function is necessary for the early detection and treatment of these patients (3). Understanding the determinants of pulmonary hypertension and right ventricular dysfunction is critical for better understanding the underlying causes of the disease and improving prognosis (4). Echocardiography, magnetic resonance imaging, and right heart catheterization can assess right ventricular function using several qualitative and quantitative parameters (3).

A resting mean arterial pressure in the lungs of 25 mmHg or higher is considered pulmonary hypertension. A patient is said to have pulmonary hypertension if their pulmonary wedge pressure is greater than 15 mmHg and pulmonary arterial resistance falls below 3 mmHg (5). It is a condition characterized by adverse remodeling of vascular beds, which in turn leads to increased vascular resistance and an overall increase in right ventricular afterload (6). It affects the arteries in the lungs and the right chambers of the heart; blood vessels in the lungs become impaired, the pressure increases, and the heart muscle becomes fragile. Pulmonary hypertension affects about 1% of people worldwide and is more common in individuals above 65 years of age (7).

Pulmonary hypertension, also known as pulmonary arterial hypertension (PAH), is a group of diseases distinguished by gradually increased pulmonary vascular resistance (PVR) and mean pulmonary arterial pressure (mPAP) due to obstructive changes in the pulmonary circulation. The parallels between different types of PAH may be due to shared underlying pathogenic mechanisms, which can eventually lead to right ventricular failure and death. Idiopathic, heritable, drug- and toxin-related conditions, tissue disorders, HIV,

Vol. 5 No. 1 (2026)

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Samad et al - 2026

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hypertension, congenital heart diseases, and schistosomiasis are all possible causes of PAH. PAH can also be caused by pulmonary veno-occlusive disease, pulmonary capillary hemangiomatosis, and persistent pulmonary hypertension in newborns. Prior to the availability of targeted therapies, the median life expectancy in PAH was less than three years, with diagnosis occurring more frequently in the 1980s. While the principles underlying PAH pathophysiology have been extensively studied over several decades, leading to the identification of numerous new therapeutic targets, many mechanisms such as vascular remodeling and raised PVR are shared by all types of pulmonary hypertension. Continuous vasoconstriction, uncontrolled remodeling of pulmonary vasculature, and thrombosis in situ are the primary mechanisms of elevated PVR in PAH (8).

Diabetes mellitus (DM) is a metabolic condition characterized by abnormally high levels of blood glucose (9). Different types of diabetes include type 1, type 2, maturity-onset diabetes of the young, gestational diabetes, neonatal diabetes, and secondary causes such as endocrinopathies or steroid use. Type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) are the two primary subtypes, often caused by defects in insulin production (T1DM) and/or action (T2DM) (10). T2DM typically affects elderly individuals with chronic hyperglycemia due to poor lifestyle and dietary choices, whereas T1DM often manifests in children or teenagers. The pathophysiology of T1DM and T2DM differs substantially, resulting in different etiologies, presentations, and treatment approaches. T1DM is defined by autoimmune destruction of pancreatic beta cells, often resulting in complete insulin deficiency. T2DM develops more subtly, with functional insulin deficits arising from an imbalance between insulin levels and insulin sensitivity, often influenced by age and fat accumulation (10).

Vol. 5 No. 1 (2026)

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The most common cause of mortality among individuals with pulmonary hypertension is right ventricular (RV) failure. Therefore, improving RV function is a crucial objective. To correct RV dysfunction and prevent RV failure, a comprehensive understanding of the pathophysiology of RV failure and the mechanisms governing the transition from a pressure-overloaded, evolving right ventricle to an enlarged, malfunctioning right ventricle is required. A failing right ventricle may exhibit abnormal metabolism, myocardial fibrosis, capillary rarefaction, and insufficient RV contractility (11).

Right ventricular hypertrophy (RVH) occurs in two forms. Adaptive RV remodeling is defined by concentric RV enlargement with preserved systolic and diastolic function, whereas maladaptive remodeling is characterized by eccentric remodeling, RV dilation, reduced RV function, and progression to RV failure. The amount of RV afterload does not determine the style of remodeling. Morphological change from adaptive to maladaptive RV may occur even while the patient's clinical status remains stable. Early detection of maladaptive RV remodeling is important therapeutically. Clinical and genetic studies are needed to determine why some individuals have a failure-prone RV while others possess a failure-resilient RV (4).

Tricuspid regurgitation (TR) affects 65–85% of the population. Mild TR may be considered normal in the context of a physiologically normal tricuspid valve (TV). Moderate to severe TR is usually pathogenic and is associated with leaflet abnormalities and annular dilatation. Primary (organic) TR arises from congenital or acquired TV abnormalities, while secondary (functional) TR is more prevalent and occurs due to pressure or volume overload in the right heart chambers. Chronic TR can result in sustained RV volume overload (12). Functional TR (FTR) may also occur in structurally normal valves, often

Vol. 5 No. 1 (2026)

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linked to left-sided cardiac or pulmonary disorders. Pulmonary hypertension-related afterload is a major mechanism for FTR, yet severe PH does not always generate significant symptoms (13).

Echocardiography is usually the first diagnostic test in dyspneic patients. Three-dimensional echocardiography can be used to measure RV volumes, though evaluating the RV remains challenging. RV assessment involves quantifying afterload and preload, with pulmonary artery systolic pressure (PASP) calculated from right atrial pressure (RAP) and TR velocity. Diastolic and mean PA pressures may also be determined using pulmonary regurgitation velocity. Vascular resistance (PVR) can be calculated if RV function is impaired. The mechanism and severity of TR are assessed, typically using the tricuspid annular plane to quantify RV performance (14).

The frequency of PAH varies, with an incidence ranging from 2.0 to 7.6 cases per million per year, corresponding to 11 to 26 instances per million adults (15). The prevalence of PH and RV dysfunction at baseline was 62.4% and 43.1%, respectively (4). Pulmonary arterial hypertension is four times more common in women than men, though survival is paradoxically worse in men (15). Patients with diabetes mellitus have a higher prevalence of pulmonary hypertension regardless of other cardiac conditions. Globally, diabetes affected 10.5% (536.6 million) of adults aged 20–79 in 2021 and is projected to rise to 12.2% (783.2 million) by 2045. Men and women have similar rates, with the highest prevalence among those aged 75–79. Almost half a billion individuals worldwide suffer from diabetes, representing over 10.5% of all adults (16). The rising prevalence of obesity has contributed to the global increase in diabetes. Diabetes remains a serious public health issue due to early morbidity, mortality, reduced life expectancy, and the associated

Vol. 5 No. 1 (2026)

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Print ISSN 3007-2379

Samad et al - 2026

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socioeconomic burden. Type 2 diabetes accounts for the majority (>85%) of cases, with type 1 diabetes comprising the remainder (9).

In both diabetic and non-diabetic patients with pulmonary hypertension, RV function is crucial for prognosis. However, due to diabetes' impact on the cardiovascular system, structural and functional changes may occur in the heart in the context of pulmonary hypertension. The evaluation of RV function in diabetic patients with pulmonary hypertension remains incompletely understood

Objectives

The main objective of our research study is;

To determine the frequency of right ventricular dysfunction in diabetic and nondiabetic patients having pulmonary hypertension.

Literature Review

Santiago Vacas et al. (2020) carried out study to determine the prognosis of pulmonary hypertension and right ventricular dysfunction in the context of heart failure. The study found that right ventricular dysfunction, which is connected to PH, has a substantial effect on heart failure individual's outcome. Understanding the causes of right ventricular dysfunction is therefore critical for patient management. The data showed that right ventricular dysfunction and PH have different trajectories that can be influenced by a variety of factors, including diabetes status. SantiagoVacas et al. (2020) emphasize the importance of right ventricular dysfunction in patients with PH, emphasizing the need for additional research addressing the role of diabetes in right ventricular function (4).

Hameed et al. (2023) provides an in-depth review of right ventricular function assessment, including its relevance in patients with PH. Their review emphasizes the

Vol. 5 No. 1 (2026)

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Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

DOI: http://doi.org/10.5281/zenodo.19016978

importance of accurate evaluation and monitoring of right ventricular function in both diabetic and non-diabetic patients (3).

Muhammad Adil Soof et.al Retrospective, cross-sectional study carried out at King Fahad medical City, Riyadh, Saudi Arabia. The study included 95 adult patients who were referred for the catheterization of right heart. The echocardiographic evaluation of PAPs and PAPm, they conclude, has a poor to moderate association with hemodynamic data and a high sensitivity. The best correlation between PAPs measurement on an echocardiography and invasive assessment is found in PAPm measurement utilizing PAPs. in individuals with moderately to severely severe TR and TAPSE (17).

This study is carried out by Sun H, Saeedi, et al. A total of 219 data sources that reported research done between 2005 and 2020 and represented 215 countries and territories were found, all of which met pre-established quality criteria. In order to project future, populace estimates for 2045 were applied to the diabetes prevalence estimates from 2021. They come to the conclusion that approximately 500 million individuals globally—or more than 10.5% of adult population—live with diabetes (16). Widya et al. (2013) used magnetic resonance imaging to compare the dimensions and role of the right ventricle (RV) in men with type 2 diabetes and a control group of healthy people in a similar age range. They also looked for any correlations between LV size and function and RV parameters. The findings of this study revealed that diabetic patients and their healthy counterparts differed significantly in RV structure and function. Furthermore, the study discovered that diabetic patients had abnormalities in the diastolic and systolic functioning of their RVs. These findings highlight the interaction between the left and right ventricles in type 2 diabetes patients, indicating that changes in the RV are mirrored

Vol. 5 No. 1 (2026)

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Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

DOI: http://doi.org/10.5281/zenodo.19016978

in the LV. As a result, this study emphasizes that RV dysfunction may be a phenotype of diabetic cardiomyopathy (18).

The review was supported by the Netherlands Heart Establishment, Dutch Diabetes Exploration Establishment, Dutch Kidney Establishment, and Eli Lilly, the Netherlands (distributed on February 12 2012). This study took a gander at the impacts of type 2 diabetes on right ventricular (RV) capability in individuals without confusions. These outcomes feature the intensive appraisal important to oversee diabetic cardiomyopathy (19).

In 2014, Stephen L. Archer of the University of Chicago and Hossein Ardehali of Northwestern University investigated how pulmonary arterial hypertension (PAH) causes right ventricular hypertrophy (RVH) and failure. The authors distinguish between adaptive and maladaptive RVH while investigating the molecular mechanisms underlying these states. Poor outcomes are associated with maladaptive RVH, which is defined by dilatation, fibrosis, and decreased angiogenesis. The transition from adaptive to maladaptive RVH is associated with metabolic changes (20).

Ayman Ahmed et al. (2011) from Mansoura University, Egypt: Department of Cardiology, Mansoura Faculty of Medicine investigated the right ventricle (RV), which is frequently overlooked in diabetic patients, providing insight into the RV's critical role in cardiac and pulmonary vascular disorders. Despite the fact that left ventricular function has been thoroughly researched and is widely accepted in clinical practice, the writers emphasize the significance of right ventricular role in a variety of patient groups. In many cases, the functioning of the RV is recognized as an important factor in determining prognosis and effort tolerance. The study emphasizes how difficult it is to assess RV

Vol. 5 No. 1 (2026)

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https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

DOI: http://doi.org/10.5281/zenodo.19016978

function due to its intricate geometry, connection to the left ventricle, and sensitivity to changes in pulmonary pressure (21).

Abernethy et al. (2015) investigated how diabetes affects people with pulmonary hypertension (PH). 21% patients out of 261 population were evaluated for pulmonary hypertension. Diabetic patients were older and had elevated right atrial pressure, and were more likely had hypertension. Diabetic patients had significantly lower survival despite similar management and functional status, emphasizing the need for additional research in this area (22).

Topilsky et al. (2012) studied the mechanism of functional TR and compared it in patients with and without pulmonary hypertension. The literature highlights the need of distinguishing idiopathic tricuspid regurgitation from pulmonary hypertension, functional tricuspid regurgitation in comprehending the complexities of functional tricuspid regurgitation. This study adds to the progress of targeted therapies and enhanced patient care in the setting of functional tricuspid regurgitation by understanding their specific clinical presentations, processes, and therapy implications (13).

Methodology

An observational cross-sectional study was conducted in the Cardiology Department of Rehman Medical Institute, Hayatabad, Peshawar. The study duration was three months. The sample size was calculated as 353 participants using the formula $n = P(1 - P)\,Z^2 / e^2$, where the confidence level (Z) was 95%, the margin of error (e) was 5%, and the estimated prevalence (P) was 64.2% based on previous studies. A simple convenient non-probability sampling technique was used for participant selection. The study included patients diagnosed with pulmonary hypertension, both with and without diabetes, and aged between 20 and 65 years. Patients with congenital heart disease and those who were non-

Vol. 5 No. 1 (2026)

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https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

DOI: http://doi.org/10.5281/zenodo.19016978

cooperative were excluded from the study. Prior to data collection, ethical approval was obtained from the Ethical Research Committee of Rehman College of Allied Health Sciences, and permission was also granted by the Graduate Student Committee of Rehman Medical Institute. Data were collected using a self-administered questionnaire after obtaining approval from the Head of the concerned department. The collected data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) version 2022 to evaluate the relationship between variables.

Results

A total of 353 participated in this study in which 63.46 were male and 36.54 were female. Data was collected through questionnaire. Both male and female diabetic and non-diabetic patients with pulmonary hypertension were included. The percentage of male patients were higher than female patients as shown in figure 1.

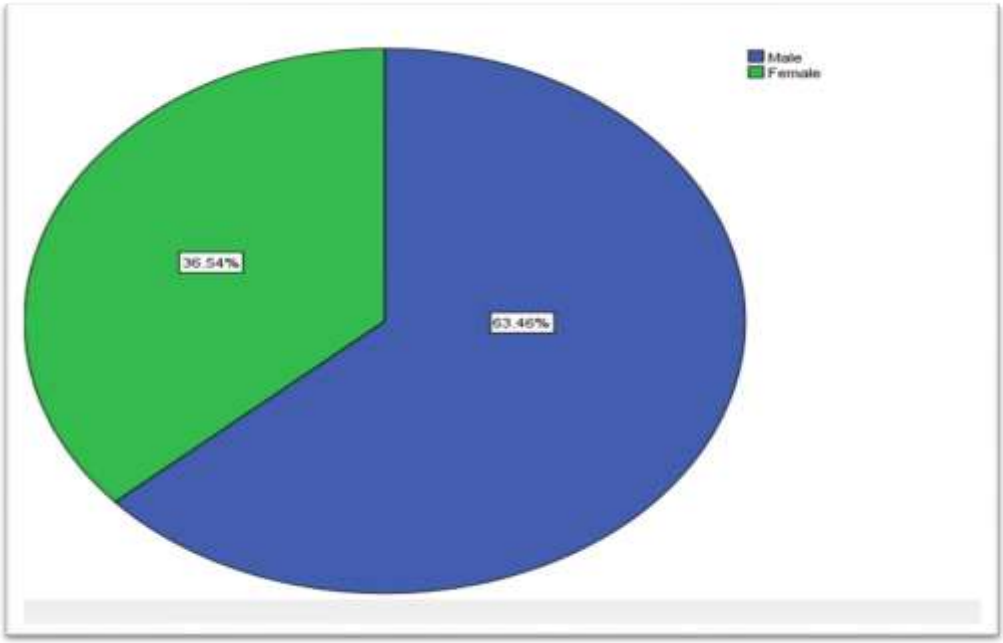

Figure.1 Gender of the patient

Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

DOI: http://doi.org/10.5281/zenodo.19016978

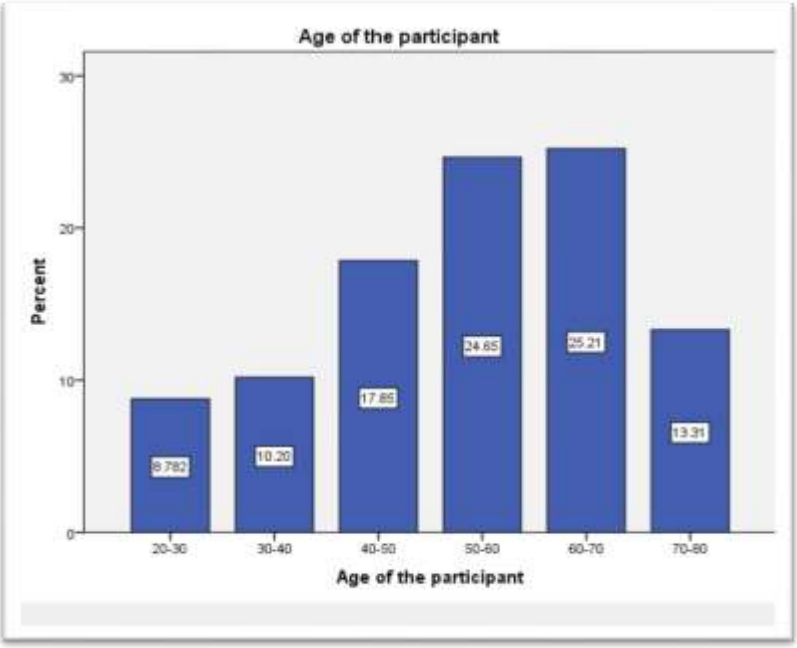

Figure.2 Age of participant

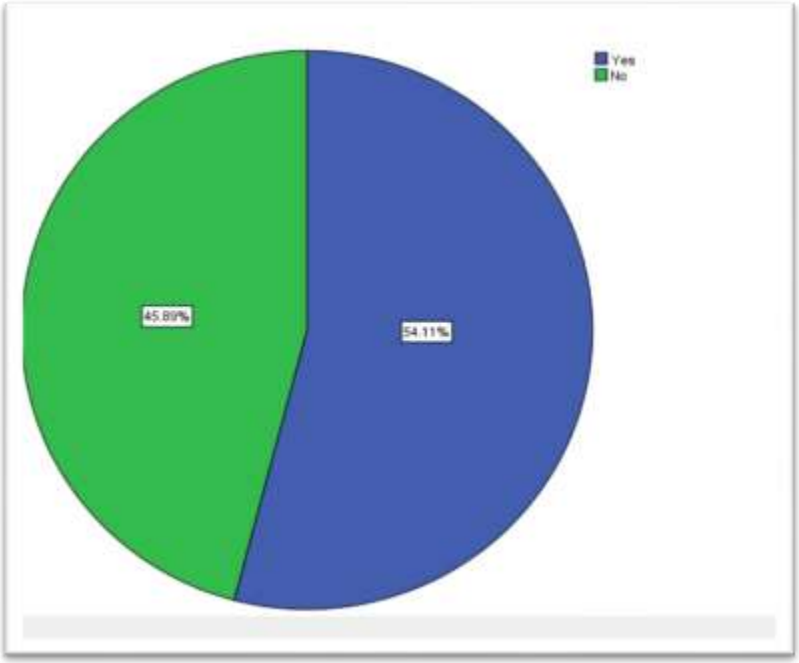

Figure. 3 Patients having diabetes

Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

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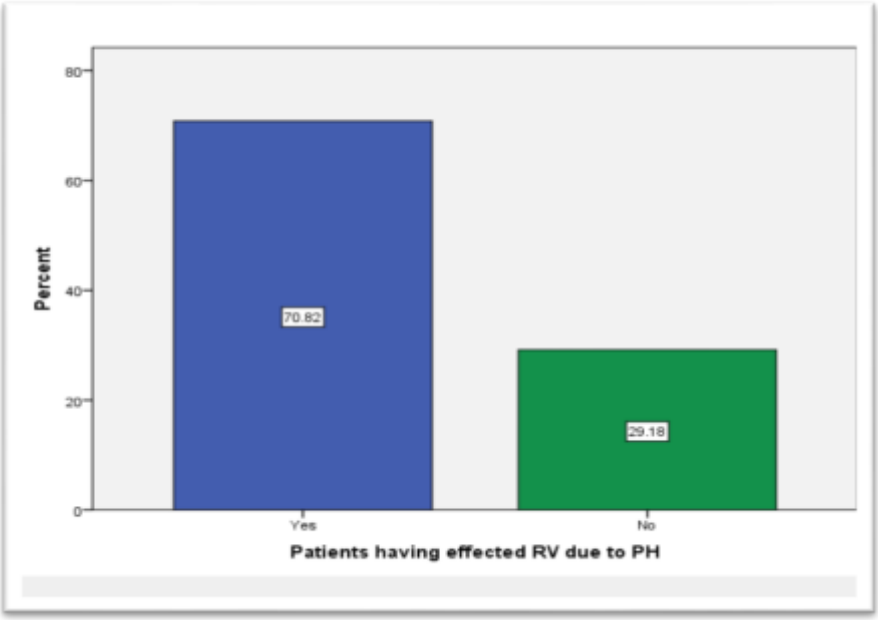

Figure. 4 Patients having impaired RV due to PH

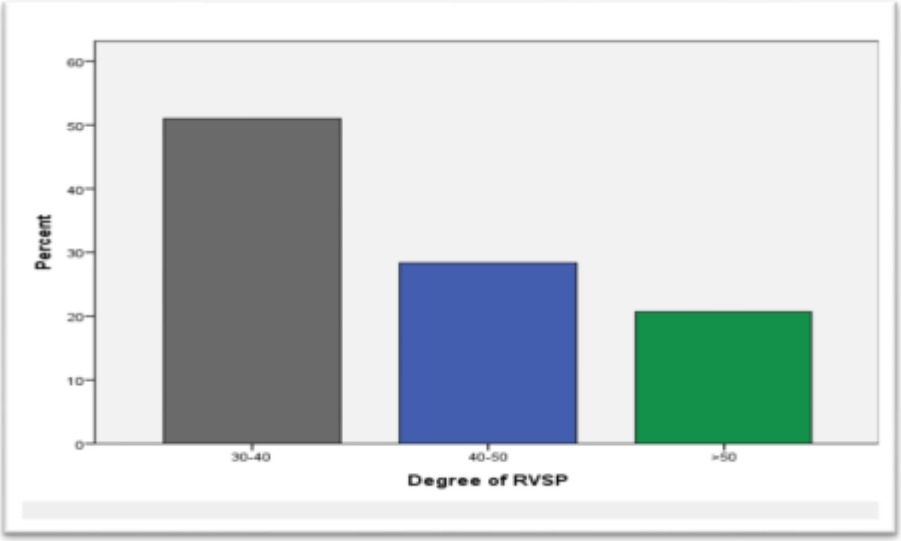

Figure.5 Degree of RVSP

Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

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Print ISSN 3007-2379

Samad et al - 2026

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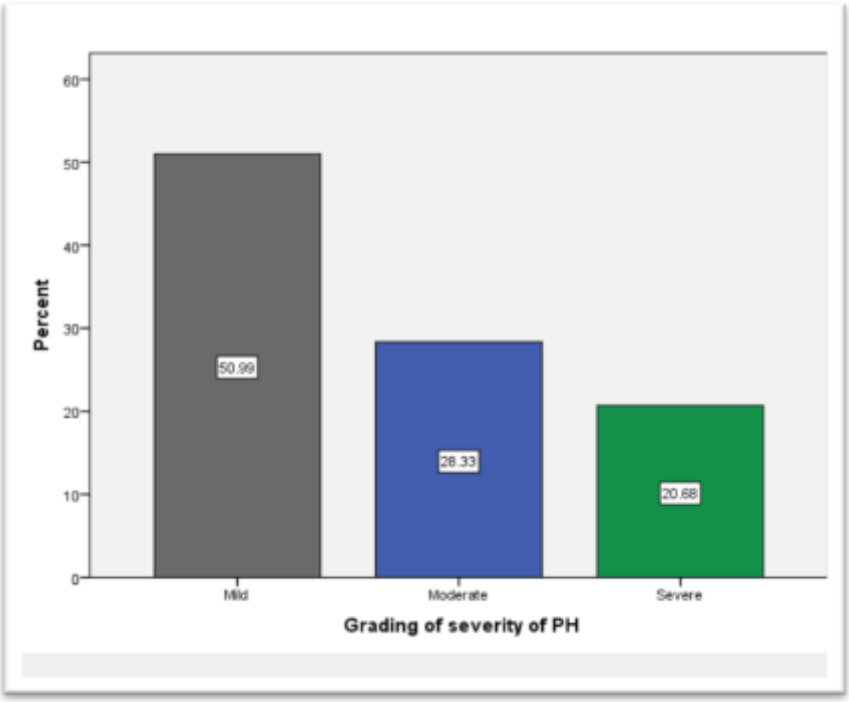

Figure.6 Grading of severity of PH

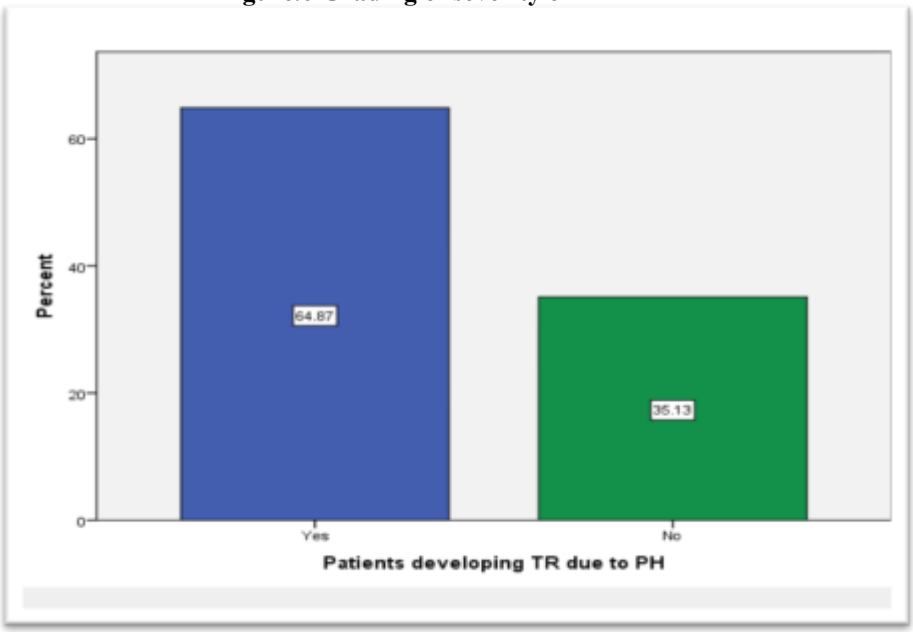

Figure.7 Patients developing RVH due to PH

Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

DOI: http://doi.org/10.5281/zenodo.19016978

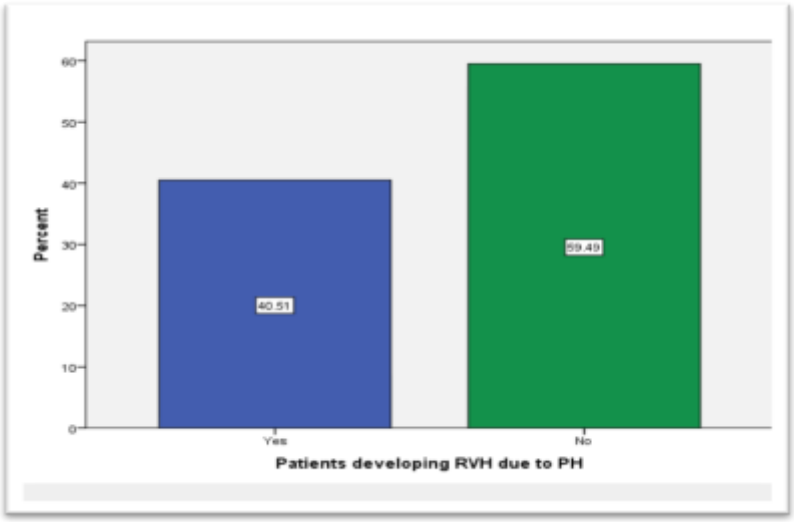

Figure.8 Patients developing TR due to PH

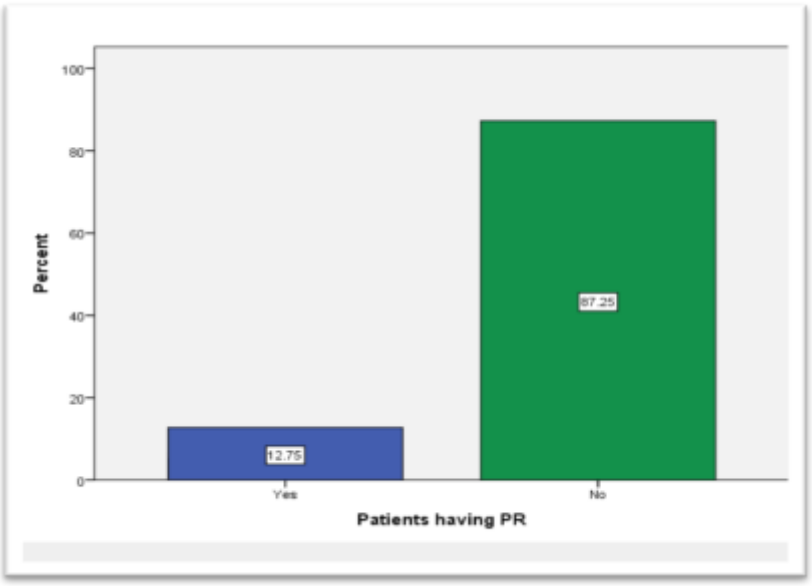

Figure.9 Patients having PR

After analyzing our data, we concluded that the patients who were diabetics and had more chances to develop right ventricular dysfunction (RVD) in terms of right ventricular

Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

DOI: http://doi.org/10.5281/zenodo.19016978

hypertrophy (RVH) and tricuspid regurgitation (TR) as compared to nondiabetic patients having pulmonary hypertension as shown in figure 12 and table 1.

Table.1 Relationship between diabetes and impaired RV

		Right Ventricular Systolic Dysfunction		Total
		Yes	No	
Patients having diabetes	Yes	158	33	191
	No	92	70	162
Total		250	103	353

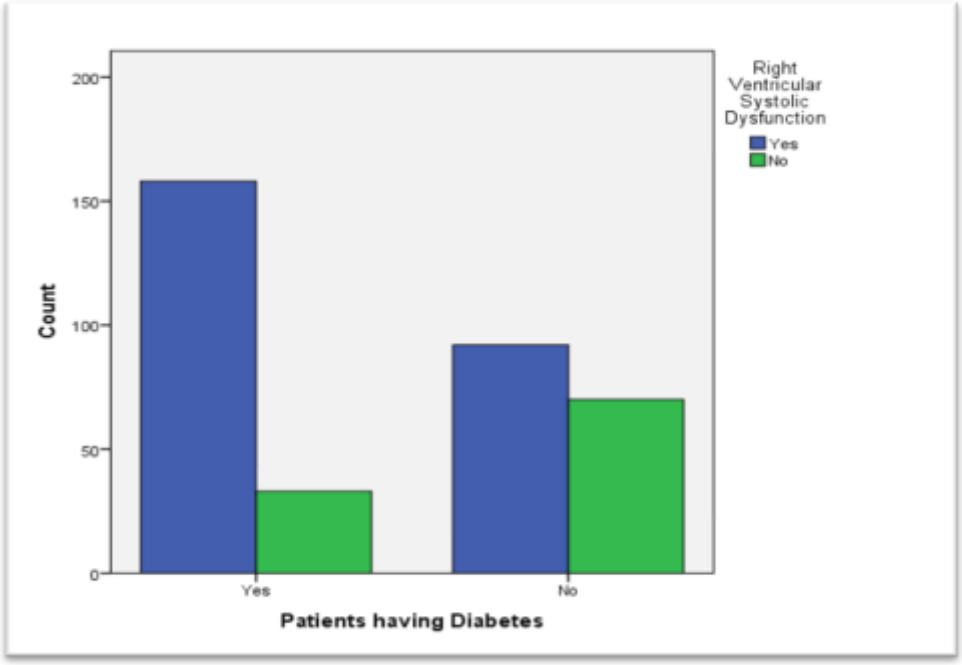

Figure.10 Relationship between diabetes and impaired RV

Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Samad et al - 2026

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Since pulmonary hypertension (PH) and RV function are closely related from a pathophysiological perspective, an evaluation of RV function must be accompanied by an assessment of pulmonary pressures. When both conditions are present, the chances of mortality vary from two to five times that of respondents (4). Hence the goal of our study is to emphasize the role of right ventricle and its relation with pulmonary hypertension in diabetic and non-diabetic patients.

We collected our primary data through questionnaires. Different factors were present like pulmonary hypertension, shortness of breath, chest pain, right ventricular hypertrophy, tricuspid regurgitation and pulmonary regurgitation.

After the collection of data, we found that right ventricle is greatly affected in diabetic individuals as compared to non-diabetic individuals having pulmonary hypertension in tertiary care hospital Peshawar i.e., Rehman Medical Institute. A total of 353 questionnaires were statistically analyzed. All the patients that we included in our study had pulmonary hypertension. We concluded that 191 patients out of 353 had diabetes while other 162 patients were non-diabetics. We also determined that ratio of right ventricular dysfunction was higher in diabetic patients as compared to nondiabetic patients.

Conclusion

The goal of this study was to observe that how many patients with diabetics and pulmonary hypertension would have their right ventricle affected in tertiary care hospital Peshawar i.e., Rehman Medical Institute. Hence this study concluded that patients with diabetes who have already existing pulmonary hypertension are more likely to develop right ventricular dysfunction as compared to non-diabetic patients.

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https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387
Print ISSN 3007-2379

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Recommendation

This study evaluates only the frequency of right ventricular dysfunction in diabetic and non-diabetic patients having pulmonary hypertension. We recommend that further studies should be carried out to find the pathophysiology and underlying mechanisms.

Limitation

We didn't determine the pathophysiology and underlying causes of RV dysfunction in diabetic patients. We only took data in which patients suffered from PH and had RV affected (i.e., TR) and then compared them in diabetic and non-diabetics. Hence, we only concluded the frequency of RV dysfunction in diabetics.

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Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387
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