Original Article

Preoperative Pulmonary Artery Hypertension

Prevalence of Preoperative Pulmonary Artery Hypertension among Patients Undergoing Mitral Valve Surgery and its Association with In-Hospital Outcomes

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ABSTRACT

Objective: Objective of the study is to determine the prevalence of preoperative Pulmonary Artery Hypertension (PAH) and its severity in patients undergoing Mitral Valve surgery at a tertiary care hospital in Karachi, Pakistan.
Study Design: Descriptive Observational study
Place and Duration of Study: This study was conducted at the Cardiac Surgery Department of National Institute of Cardiovascular Diseases (NICVD) Karachi for a period of six months December 2020 to May 2021.
Materials and Methods: Non-probability, Consecutive Sampling. Patients fulfilling the inclusion criteria were included in this study, Patients diagnosed with Mitral Regurgitation (MR) or Moderate to Severe Mitral Stenosis (MS) undergoing mitral valve surgery. Pulmonary Artery Hypertension was labelled PAH [+] if preoperative systolic pulmonary artery pressure (sPAP) ≥ 40 mmHg, as measured with Doppler echocardiography, otherwise it was labelled as PH [-]. Data was entered and analysis using SPSS version-21. Variables was expressed using appropriate descriptive statistics such as mean ± SD, median (IQR), maximum and minimum. Frequency and percentages were calculated for categorical variables.
Results: During this period of study 68 patients were included in study who were operated for Mitral Valve Replacement(MVR). It included 50(74%) females and 18 males (26%).In these patients only 1(1.4%) was operated through minimally invasive mitral valve replacement whereas 67(98.52%) patients with conventional mitral valve replacement (MVR) through median sternotomy. All the patients who were operated had severe disease. Pulmonary Artery hypertension (PAH) was present in 23(74.2%) out of 33 Mitral Regurgitation (MR) patients. Pulmonary Artery hypertension (PAH) was present in 23(74.2%) out of 31 patients who had Mitral Stenosis MS. Overall In-hospital mortality in our study was 10.3% (7 out of 68 patients).
Conclusion: Prevalence of PAH is high in patients undergoing Mitral Valve Replacement surgery. Major factors associated with post-operative mortality include prolonged ICU stay, prolonged ventilation and need for high inotropic support.
Key Words: Pulmonary Artery Hypertension (PAH), Mitral Valve surgery, MS, MR

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INTRODUCTION

Rheumatic heart disease (RHD) has almost been eradicated from the developed countries but it still poses a major health concern in developing countries.

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A significantly large number of young adults suffer from morbidity and mortality related to the involvement of mitral and aortic valves[1]. RHD most commonly affects mitral valve leaflets and sub valvular apparatus causing Mitral Stenosis (MS) Mitral Regurgitation (MR) and Mixed disease, both MS and MR.

Pulmonary Artery Hypertension (PAH) describes a vast array of disease states in which chronically elevated pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR) ultimately result in right heart failure (RHF) and death.[(2)] Pulmonary Artery hypertension (PAH) may occur with the gradual progression of mitral regurgitation (MR) in patients with mitral valve (MV) prolapse and cardiac surgical patients presenting with pre-existing PAH are at a higher risk for postoperative complications and it has been reported to have negative impact on operative outcomes.[(1–5)] In well known risk scoring system,

European System for Cardiac Operative Risk Evaluation II (EuroSCORE II), PAH is considered a risk factors for mortality[6].

Current American College of Cardiology/American Heart Association and European Society for Cardiology guidelines recommend surgery for asymptomatic patients with MR and resting systolic pulmonary artery pressure (sPAP) greater than 50 mmHg as a class II a recommendation based on level C evidence.[7,8]

A recent retrospective observational study on Pakistani population by Chaudhri MS et al. [8] observed significant reduction of PAH postoperatively and concluded that the Mitral valve replacement in the presence of severe PAH is a safe procedure. Study further reported that the mean cardiopulmonary bypass and aortic cross clamp times were 89.87±23.15 and 62.48±18.75 minutes respectively. Mean ventilation time was 7.13±5.65 hours while the mean inotropic requirement was 30.22±23.12 hours. There was no peri-operative mortality.[8]

Ghoreishi M et al. [5] reported preoperative PH (sPAP > 40 mmHg) in 53% of the patients with mild in 20%, moderate in 16% and severe PH in 17% of the patients. Study further reported that preoperative PH was strongly associated with operative mortality (p-value <0.001) with mortality rate of 2% for patients with no PH, 3% for patients with mild, 8% for moderate, and 12% for those with severe preoperative PH. Higher preoperative sPAPs were associated with higher rates of prolonged ventilation (p-value <0.001), longer hospital stay (p-value <0.001), intensive care unit stay more than 24 hours (p-value 0.021), and dialysis (p-value 0.009).

However, there is no consensus about the outcome of patients with PAH after MVR in the literature [10], some studies have revealed that severe PAH is associated with poorer outcome and higher mortality rate [1-5] while some others do not agree with this and believed that severe PAH do not imply the greater risk in corrective surgery. [11, 12] Although pulmonary artery hypertension has been reported as a major predictor of adverse cardiovascular events, there are limited studies on its association with operative morbidity and mortality for patients undergoing Mitral Valve surgery especially in our population. Therefore, it is imperative to study the impact of preoperative PAH on operative outcome of Mitral Valve surgery in our population so that better patient management strategies could be devised.

MATERIALS AND METHODS

It is Descriptive Observational study conducted in Cardiac Surgery Department of National Institute of Cardiovascular Diseases (NICVD) Karachi. Duration of Study was Six months

Sampling Technique: Non-probability, Consecutive Sampling**.** Patients fulfilling the following criteria were included in this study; 1-Age between 16 to 75 years 2-Either gender 3-Patients diagnosed with Mitral Regurgitation (MR) or Moderate to Severe Mitral Stenosis (MS) undergoing mitral valve surgery (as per the operational definition). Patients who were excluded from this study ; 1-Patients with prior history of any cardiac related surgery 2-Patients refused to give consent.

Mitral Regurgitation (MR) was classified as "Severe", "Moderate", and "Mild" based on echocardiography findings as per the following criteria; Mild Mitral Regurgitation (MR): Mild MR was defined as, Small central jet <4 cm^2 or <20% of LA area, Vena contracta width < 0.3cm, regurgitant volume between 30 to 44 ml/beat, regurgitant fraction between 30 to 39%, and effective regurgitant orifice area between 0.20 to 0.29 cm^2. Moderate Mitral Regurgitation (MR): Moderate MR was defined as, signs of MR>mild present, but no criteria for severe MR with regurgitant volume between 45 to 59 ml/beat, regurgitant fraction between 40 to 49%, and effective regurgitant orifice area between 0.30 to 0.39 cm^2. Severe Mitral Regurgitation (MR): Severe MR was defined as, Vena contracta width ≥ 0.7cm with large central MR jet (area < 40% of LA) or with a wall-impinging jet of any size, swirling in LA, regurgitant volume ≥ 60 ml/beat, regurgitant fraction ≥ 50%, and effective regurgitant orifice area ≥ 0.40 cm^2.

Moderate to Severe Mitral Stenosis (MS): MS was classified as "Severe", "Moderate", and "Mild" based on echocardiography findings as per the following criteria; Mild Mitral Stenosis (MS): Mild MS was defined as, valve area > 1.5cm^2 with supportive finding of mean gradient < 5 mmHg and pulmonary artery pressure <30 mmHg.Moderate Mitral Stenosis (MS): Moderate MS was defined as, valve area between 1 to 1.5cm^2 with supportive finding of mean gradient between 5 to 10 mmHg and pulmonary artery pressure between 30 to 50 mmHg.Severe Mitral Stenosis (MS): Severe MS was defined as, valve area < 1.0cm^2 with supportive finding of mean gradient > 10 mmHg and pulmonary artery pressure >50 mmHg.

Pulmonary Artery Hypertension (PAH): Patients was labelled PAH [+] if preoperative systolic pulmonary artery pressure (sPAP) ≥ 40 mmHg, as measured with Doppler echocardiography, otherwise it was labelled as PH [-]. Severity of preoperative Pulmonary Artery Hypertension (PAH) was categorized as: No Pulmonary Hypertension***:*** sPAP < 40 mmHg**,** Mild Pulmonary Hypertension: 40 mmHg ≤ sPAP < 50 mmHg**,** Moderate Pulmonary Hypertension: 50 mm Hg ≤ sPAP < 60 mmHg and Severe Pulmonary Hypertension: sPAP ≥ 60 mmHg.

In-hospital Outcome: included the following Mortality: was labeled as "Yes" if patients died within 7 days of hospital stay after the surgery, otherwise, was labeled as "No". Prolonged Intensive Care Unit (ICU) stay: was labeled as "Yes" if ICU stay was more than 48 hours, otherwise, will be labeled as "No". Prolonged

ventilation: was labeled as "Yes" if more than 24 hours, otherwise, it was labeled as "No". Inotropic Support: was labeled as "Yes" if lasting for more than 24 hours, otherwise, it was labeled as "No". Long Cardiopulmonary Bypass (CPB) Time: was labeled as "Yes" if more than 240 minutes, otherwise, it was labeled as "No".

Diabetic Mellitus (DM): was labelled as "Yes" for the patients with documented history of DM and on anti-diabetic medication for at least 6 months. Hypertension (HTN): will be labelled as "Yes" for the patients with documented history of HTN and on anti-hypertensive medication for at least 6 months. Smoking: was labelled as "Yes" if patient has history of smoking 10 to 20 cigarettes per day for last 5 years otherwise it was labelled as "No".

Data Collection and Analysis: The study was started after approval from the ethical review committee of NICVD. For this study we included consecutive patients undergoing mitral value surgery and fulfilling the inclusion criteria at cardiac surgery department, NICVD, Karachi. Prior to inclusion, the purpose and benefits of the study were explained to all the participants and informed consent was taken by the principal investigator from all patients. Patient's demographic data was obtained such as Age (years) and gender. History of the patients was taken, as per the operational definitions, regarding diabetic mellitus, hypertension, and smoking status. Echocardiography was performed by echo cardiographers with work experience of more than five years for all the patients. Severity of mitral stenosis (MS) and mitral regurgitation (MR) was assessed as per the operational definitions. Preoperative systolic pulmonary artery pressure (sPAP) was measured using modified Bernoulli equation;

4x [tricuspid regurgitation jet velocity]^2 + right atrial pressure [10 mmHg].

And preoperative pulmonary artery hypertension (PAH) and its severity was assessed as per the operational definitions. Mitral valve surgery in all the patients was performed by the surgeon having minimum 5 years of experience. Patients were observed during their hospital stay and in-hospital, intra operative and post-operative outcomes were recorded and measured as per the operational definitions such as mortality, prolonged intensive care unit (ICU) stay, prolonged ventilation, inotropic support, long cardiopulmonary bypass (CPB) time, and long aortic clamp time. All the collected data was recorded on predesigned proforma. Confounding variables and biasness were controlled by strictly following inclusion and exclusion criteria and stratification. Patient information was kept secured and was available to authorized person only.

Data was entered and analysis using SPSS version-21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Variables such as age (years), systolic pulmonary artery pressure (sPAP mmHg), intensive care unit (ICU) stay (hours), ventilation (hours), inotropic support (hours), cardiopulmonary bypass (CPB) time (hours), and aortic clamp time (hours). Quantitative (continuous) variables was expressed using appropriate descriptive statistics such as mean ± SD, median (IQR), maximum and minimum. Frequency and percentages were calculated for categorical variables such as gender, age group, diabetic mellitus, hypertension, smoking status, severity of mitral regurgitation (MR), severity of mitral stenosis (MS), pulmonary hypertension (PH), severity of pulmonary hypertension (PH), and in-hospital intra operative and post-operative outcomes (mortality, prolonged intensive care unit (ICU) stay, prolonged ventilation, inotropic support, long cardiopulmonary bypass (CPB) time, and long aortic clamp time). Effect modifiers like gender, age group, diabetic mellitus, hypertension, smoking status, severity of mitral stenosis (MS), and severity of mitral regurgitation (MR) were controlled through stratification.

RESULTS

During this period of study 68 patients were included in study who were operated for Mitral Valve Replacement(MVR). It included 50(74%) females and 18 males (26%).In these patients only 1(1.4%) was operated through minimally invasive mitral valve replacement whereas 67(98.52%) patients with conventional mitral valve replacement (MVR) through median sternotomy. Redo- MVR surgery was done in 4(5.9%) patients. Emergency MVR was done in 1(1.4%) patient who developed sudden onset of shortness of breath after Percutaneous Mitral Balloon Valvuloplasty (PMBV) and developed severe MR and was intubated before shifting to operation theatre.

Table No.1: Effect modifiers in the study population

	Yes	No
Diabetes Mellitus	03	65
Hypertension	20	48
Smoking	05	63

All the patients who were operated had severe disease.

Table No.2: Distribution of severity of Mitral valve disease

Mitral valve pathology	Mild	Moderate	Severe
MR	00	00	33
MS	00	00	31
MR+MS	00	00	04

Pulmonary Artery hypertension (PAH) was present in 23(74.2%) out of 33 Mitral Regurgitation (MR) patients. In MR patients PAH was severe in 7(30.4%), 6(26.1%) patient had moderate PAH, 10(43.5%).

Pulmonary Artery hypertension (PAH) was present in 23(74.2%) out of 31 patients who had Mitral Stenosis MS. In these MS patients 9(39.1%) had severe

PAH,6(26.1%) patients had moderate PAH and 8(34.8%) patients had mild PAH. All 4(100%) patients who had mixed disease (MR+MS) has PAH and it was severe in intensity.

In-hospital, intraoperative and postoperative outcomes are listed in tables 3, 4, 5.

Table No.3: In hospital, intraoperative and postoperative outcomes in MR patients

Outcomes	Yes	No
Long CPB	00	33
Long aortic clamp time	00	33
Mortality	03	30
Prolonged ICU stay	31	02
Prolonged ventilation	05	28
Inotropic support	31	02

Table No.4: In-hospital, intraoperative and postoperative outcomes in MS patients

Outcomes	Yes	No
Long CPB	01	30
Long aortic clamp time	01	30
Mortality	04	27
Prolonged ICU stay	25	06
Prolonged ventilation	03	28
Inotropic support	29	02

Table No.5: In-hospital, intraoperative and postoperative outcomes in Mixed Mitral valve disease patients

Outcomes	Yes	No
Long CPB	00	04
Long aortic clamp time	00	04
Mortality	00	04
Prolonged ICU stay	04	00
Prolonged ventilation	00	04
Inotropic support	04	00

DISCUSSION

Rheumatic heart disease remains the most common cause of valvular heart disease in developing countries.[1] Pulmonary artery hypertension (PAH) is a long term sequelae of mitral valve disease in these patients. The mechanism by which PH develops in patients with mitral valve disease is driven by an elevation of LA pressure, which in turn, leads to pulmonary venous hypertension, and subsequently, pulmonary arterial hypertension.[14,17,18] In our study, PAH was present in 50 out of 68 patients (73.5%). Borde et al reported prevalence of severe PAH to be 40% in a similar study. Whereas, the prevalence of severe PAH was 29.4% in our study population.

Overall In-hospital mortality in our study was 10.3% (7 out of 68 patients).Cesnjevar et al[16] and Mubeen et al[13] reported 10.5% and 9.3% mortality respectively, which is similar to our results. Out of these 7 mortalities in our study group, 3 patients had mild PAH, 3 had moderate PAH and only 1 patient had severe PAH. Mortality was highest in moderate PAH group, which was 25%.

Factors significantly associated with mortality were prolonged ICU stay, prolonged ventilation and use of high inotropic support. Long CPB time and long aortic cross-clamp time has no impact on mortality of these patients.

PAH prevalence is high in patients undergoing Mitral valve surgery especially patients with Mixed Mitral valve disease and mitral regurgitation. These patients impose a challenge to the surgeons, anesthetists and intensivists. However, these patients can be managed effectively with a team based approach paying close attention to pre-op, intra-op and post operative care.

CONCLUSION

Prevalence of PAH is high in patients undergoing Mitral valve Replacement surgery. Major factors associated with post-operative mortality include prolonged ICU stay, prolonged ventilation and need for high inotropic support.

Author's Contribution:

Concept & Design of Study:	Asmatullah
Drafting:	Romana Awan,
Data Analysis:	Muhammad Arif, Ishaq Khan
Revisiting Critically:	Abdul Wasay
Final Approval of version:	Muhammad Asad Bilal Awan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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