

# The Burden of Pulmonary Hypertension in Patients with Degenerative Mitral Valve Disease in Enugu South-East Nigeria: An Echocardiographic Based Study

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## Abstract

**Background:** Pulmonary hypertension is a common complication of degenerative mitral valve disease, and contributes significantly to both morbidity and mortality. The use of medications for reduction of pulmonary pressure in patients is not a common practice by most physicians in this part of the world because of the absence of data on pulmonary hypertension. **Aim:** The authors set out to find the prevalence of pulmonary hypertension in patients with degenerative mitral valve disease and to determine if there are gender differences in affectation. This will form a basis for future research on the management of pulmonary hypertension in sub-Saharan Africa. **Subjects and Methods:** The echocardiographic records of 1390 patients carried out over a period of 4 years were retrospectively reviewed. The examinations were done with a Logic 500 MD echocardiographic machine. Tricuspid valve regurgitation velocity above 250 cm/s defined pulmonary hypertension. Data obtained included presence of degenerative mitral valve disease, pulmonary hypertension, age, and gender. **Results:** A total of 1390 echocardiogram reports done at Conquest Medical Imaging, Enugu, from July 2009 to August 2013 were retrospectively reviewed. Degenerative mitral valve disease was noted in 18.7% of the patients, (259/1390) made up of 149 males and 110 females with a mean age of 68.3 (14.4) years. Pulmonary hypertension was present in 30% of the patients (78/259) and affected males more than females. **Conclusion:** Pulmonary hypertension is common in patients with degenerative mitral valve disease in Enugu, and affects males more than females.

**Keywords:** Degenerative mitral valve disease, Nigeria, Pulmonary hypertension

## Introduction

The most common cause of pulmonary hypertension is left sided heart disease resulting in venous pulmonary hypertension. Echocardiography allows for assessment of left ventricular systolic and diastolic dysfunction as well as left-sided valvular disease and congenital heart disease.<sup>[1]</sup> Primary degenerative mitral valve regurgitation is a frequent and serious valvular heart disease that may progressively and insidiously lead to pulmonary

hypertension.<sup>[2,3]</sup> Degenerative disease is the most common form of organic mitral valve disease in the United States (with an estimated incidence of 2–3%),<sup>[4]</sup> and in other developed countries. Degenerative valvular heart diseases are the most common echocardiographic abnormalities in the elderly population in South-East Nigeria.<sup>[5]</sup> Normal mean pulmonary artery (PA) pressure ranges from 8 to 20 mmHg at rest. Pulmonary

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**How to cite this article:** Ejim EC, Oguanobi NI. The burden of pulmonary hypertension in patients with degenerative mitral valve disease in Enugu South-East Nigeria: An echocardiographic based study. *Ann Med Health Sci Res* 2016;6:172-5.

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10.4103/2141-9248.183945

hypertension is defined as mean PA pressure exceeding 25 mmHg at rest as measured by right heart catheterization.<sup>[6]</sup>

Echocardiographic estimates of PA pressures are almost always made based on a measure of the tricuspid regurgitation jet velocity, which appears to be measurable in the overwhelming majority of, though not all, patients.<sup>[7]</sup> A number of studies have examined the sensitivity of echocardiography for the diagnosis of pulmonary hypertension, using cardiac catheterization as a gold standard. These studies have found sensitivities ranging from 79% to 100%.<sup>[8,9]</sup> Furthermore, most studies have found excellent correlations between PA pressure estimated by echocardiography and that measured by catheterization.<sup>[10]</sup> The most commonly used modality to estimate PA systolic pressure (PASP) is Doppler echocardiography. PASP can be determined by measuring the peak systolic pressure gradient from the right ventricle to the right atrium.<sup>[11]</sup> This is calculated using the modified Bernoulli equation:  $4V^2$ , where  $v$  is the maximum velocity of the tricuspid valve regurgitant jet, measured by continuous wave Doppler, added to the estimated right atrial pressure.<sup>[10]</sup>

There is a dearth of data on all aspects of pulmonary hypertension in sub-Saharan Africa, and the authors set out to find the frequency and burden of pulmonary hypertension in patients with degenerative mitral valve disease diagnosed by transthoracic echocardiography.

## Subjects and Methods

Conquest Medical Imaging is a private medical diagnostic center in Enugu, South-East Nigeria. The center offers radiologic and ultrasonographic diagnostic services. The echocardiographic records of 1390 patients done over a 4-year period (July 2009–August 2013) were retrospectively reviewed. The examinations were done with a Logic 500 MD echocardiographic machine made by General Electric (GE: New York). The machine has the capability for two-dimensional, M-mode, and Doppler examinations, and is equipped with an inbuilt printer. The studies were done on outpatients who came to the private facility. Our institutional ethical committee approved the study patients with a clinical diagnosis of sleep apnea, chronic obstructive airway disease or obesity on their request form were excluded from the study. Hypertensive patients who were referred for echocardiographic examination were included in the study. Patients with rheumatic heart disease, congenital heart diseases were also excluded. All other patients with degenerative mitral valve disease were included in the study. Tricuspid valve regurgitant velocity above 250 cm/s defined pulmonary hypertension.<sup>[11]</sup> Data obtained included presence of degenerative mitral valve disease, pulmonary hypertension, age, and gender.

Data were presented as means (standard deviation) for continuous variables and as proportions for categorical variables. Comparison of continuous variables between groups (male and female) was made with independent Student's  $t$ -test. For discrete variables, distribution between groups was compared with Chi-square test and Fisher's exact test as appropriate (where an expected cell

is  $<5$ ). Age-related differences in the prevalence of pulmonary hypertension among patients with mitral valve disease were evaluated using Chi-square for trend. All statistical analyses were carried out using the Statistical Packages for Social Sciences (SPSS Inc., Chicago Illinois, USA) software version 16.0. Statistical tests with two-tailed  $P < 0.05$  were considered statistically significant.

## Results

There were 1390 echocardiogram reports over the study period. Degenerative mitral valve disease was noted in 259 patients (18.7%), made up of 149 males and 110 females with a mean age of 68.3 (14.4) years. The mean age of the females was 71.7 (12.3) years while the mean age of the males was 68.4 (10.2) years. Pulmonary hypertension was present in 78 patients, representing 30% of the study population, and made up of 47 males and 31 females. Pulmonary hypertension was noted in about 31.5% (47/149) of all the males with degenerative mitral valve disease while about 28.2% (31/110) of the females with degenerative mitral valve disease had pulmonary hypertension. Severe pulmonary hypertension (PA pressure of  $>50$  mmHg),<sup>[10]</sup> was noted in most patients with Grade 4 mitral regurgitation (MR) on color flow mapping. The differences were statistically significant ( $\chi^2 = 15.844$ ;  $df = 1$ ,  $P = 0.001$  [McNemar test]). The prevalence of pulmonary hypertension in patients with mitral valve disease increased progressively with advancing age of the patients, ( $\chi^2$  for trend = 4.1000;  $P = 0.043$ ). The mean age of the males with pulmonary hypertension was 70.4 (11.1) years while the mean age of the females was 66.9 years, and the differences were statistically significant ( $P = 0.038$ ).

## Discussion

Our study documented a frequency of 30% for pulmonary hypertension among the study population. This is definitely higher than the frequency of 15% reported by Magne *et al.*<sup>[12]</sup> The higher frequency in our study may be due to the relatively older population in our study sample. Over 50% of subjects in our study population aged 85 years and above had pulmonary hypertension [Table 1]. Resting systolic pulmonary pressure

**Table 1 : Age and gender distribution of pulmonary hypertension in patients with mitral valve disease (MVD)**

Age Range	Number with MVD	Number with Pulm Hypertension	Males with Pulm Hypertension (n=149)	Females with Pulm Hypertension (n=110)
50-54	13	5 (38.46%)	3	2
55-59	20	2 (10.00%)	0	2
60-64	35	7 (20.00%)	5	2
65-69	42	14 (33.33%)	7	7
70-74	72	19 (26.38%)	9	10
75-79	36	14 (38.89%)	11	3
80-84	26	9 (44.62%)	6	3
85-89	12	6 (50.00%)	4	2
90-94	1	1 (100.00%)	1	0
95-100	2	1 (50.00%)	1	0

**Table 2: Age and gender differences in occurrence of pulmonary hypertension in patients with mitral valve disease.**

Age Range	Number with MVD	Number with Pulm Hypertension	Males with Pulm Hypertension	Females with Pulm Hypertension
50-59	33 (12.74%)*	7 (21.21%)*	3 (2.01%) <sup>a</sup>	4 (3.64%) <sup>b</sup>
60-69	77 (29.73%)*	21 (27.27%)*	12 (8.05%) <sup>a</sup>	9 (8.18%) <sup>b</sup>
70-79	108 (41.70%)*	33 (30.56%)*	20 (13.42%) <sup>a</sup>	13 (11.82%) <sup>b</sup>
80-89	38 (14.67%)*	15 (39.47%)*	10 (6.71%) <sup>a</sup>	5 (4.55%) <sup>b</sup>
90-100	3 (1.16%)*	2 (66.67%)*	2 (1.343%) <sup>a</sup>	0 (0.00%) <sup>b</sup>
Total	259 (100.00%)	78 (30.00%)	47 (31.54%) <sup>a**</sup>	31 (28.18%) <sup>b**</sup>

\*Statistically significant age related difference in occurrence of pulmonary hypertension ( $\chi^2$  for trend=4.1000;  $P=0.0429$ ), \*\*statistically significant sex differences in occurrence of pulmonary hypertension ( $\chi^2=15.844$ ;  $df=1$ ,  $P=0.0001$  (McNemar test)), <sup>a</sup>expressed as percentage of the total number of males with mitral valve disease ( $n=149$ ), <sup>b</sup>expressed as percentage of the total number of females with mitral valve disease ( $n=110$ )

and pulmonary hypertension are known to increase with age.<sup>[13]</sup> Pulmonary hypertension frequency increased progressively with age in our study, and the highest frequency of 67% was noted in individuals aged 90 years and above [Table 2]. This is also in keeping with the findings of Magne *et al.*<sup>[12]</sup>

On analysis for gender differences in affectation, pulmonary hypertension was significantly more prevalent in males than females [Table 2]. Related studies done elsewhere in the past have also made similar observations, and reported a higher prevalence rate in males than females.<sup>[12]</sup> The reason for this may not be readily obvious, but could also be explained by the significantly older male population in our study.

Our findings suggest that degenerative mitral valvular heart disease is a frequent etiology of pulmonary hypertension. This may result from multiple mechanisms such as an increase in pulmonary vascular resistance, pulmonary blood flow, or pulmonary venous pressure. The chronic rise in pulmonary arterial pressure often leads to right ventricular pressure overload and subsequent right ventricular failure. When present, pulmonary hypertension is a marker of poor outcome in valvular heart disease.

Several studies have demonstrated the negative implications of pulmonary hypertension on the natural history and perioperative outcomes in mitral valve disease.<sup>[14-16]</sup> Yang *et al.* demonstrated that preoperative pulmonary hypertension (PASP >30 mmHg) is associated with significant reduction in postoperative left ventricular ejection fraction (LVEF) in patients with degenerative MR and normal preoperative LVEF.<sup>[14]</sup>

Similarly, another large, multicenter, international study also demonstrated that pulmonary hypertension in patients with MR approximately doubles the risk of heart failure and death after diagnosis and that surgery does not completely abolish the risk of adverse events once pulmonary hypertension is established.<sup>[15]</sup>

In a large, single-center study, Ghoreishi *et al.*, showed that, in patients with degenerative MR and pulmonary hypertension (PASP >40 mmHg) undergoing mitral valve surgery (98% underwent mitral valve repair), even mildly

elevated preoperative PASP correlated with increased operative mortality, postoperative left ventricular dysfunction, as well as long-term mortality.<sup>[16]</sup>

A major challenge in this study was addressing the confounding effects of cardiac co-morbidities. We endeavored to exclude echocardiographic data from patients with a history of hemoglobinopathies, diabetes mellitus as well as echocardiographic records suggestive of concomitant cardiac morbidities. However, the limitation resulting from the failure to fully account for the contribution of all co-morbidities likely to affect pulmonary pressure in this study is acknowledged.

## Conclusion

Pulmonary hypertension is common in middle-aged and elderly patients with degenerative mitral valve disease presenting for echocardiography in South-East Nigeria, and it is more common in males than females. Assessment of the presence and severity of pulmonary hypertension has an important role in the risk stratification and therapeutic management of degenerative mitral valve disease.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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