

Original Article

Aetiology and Clinical Profile of Giant Left Atrium – An Observational Study

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Abstract:

Key Words :

Left Atrium, Dilatation, Transthoracic Echocardiography, Aetiology, Thrombus.

Background: The predominant cause of giant left atrium (GLA) is rheumatic mitral valvular disease. GLA is commonly defined echocardiographically by measuring the left atrial diameter (LAD). In the context of changing epidemiology of rheumatic heart disease (RHD) globally, and introduction of left atrial volume index (LAVI), the aetiology of GLA and utility of LAVI for defining GLA may be necessary.

Methods: The prospective observational study was carried out at a dedicated tertiary care cardiac centre of a developing country to know the aetiology and clinical pattern of GLA over 8 years. GLA was defined echocardiographically as a left atrium (LA) having a diameter ≥ 80 mm in the left parasternal long-axis view. Follow-up was made over the telephone.

Results: Thirty cases of GLA were diagnosed over 8 years from 2013 to 2021. Twenty two were due to rheumatic heart disease (RHD), 7 due to MVP, and 1 due to flail anterior mitral leaflet. Mean LAD was 92.13 ± 16.72 mm, and the mean LAVI was 288.77 ± 134.40 ml/m². LA thrombus was present in 5 patients, 6 had spontaneous echo contrast (SEC) in LA, 2 had both LA thrombus and SEC. Mean follow-up was 0.99 ± 1.06 years. Out of 15 patients, 5 died, while 10 were alive. Mean survival was 1.8 ± 1.17 years, ranging from less than 1 year to 4 years.

Conclusion: RHD continues to be the predominant cause of GLA; however, MVP is also important. The cut-off value of LAVI for defining GLA needs further study.

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Introduction:

Giant left atrium (GLA) is a rare condition with a reported prevalence of only 0.3–0.6%.¹⁻⁴ It has variably been defined as a left atrium (LA) having a cardiothoracic ratio (CTR) of ≥ 0.7 in chest x-ray, or left atrial diameter (LAD) of ≥ 65 mm or ≥ 80 mm in transthoracic echocardiography (TTE).^{2,4} It is typically found in rheumatic mitral valvular disease (MVD), but has also been described in association with a myriad of non-rheumatic conditions.^{1,2,5}

Globally, over the past decades, the epidemiology of rheumatic fever and rheumatic heart disease (RHD) has changed considerably with a marked decline in prevalence^{6,7}, and hence, the aetiology of GLA might change accordingly. Irrespective of the underlying aetiology, the clinical importance of GLA lies in its potential for causing heart failure, compression effect on the nearby structures, atrial fibrillation (AF), and facilitating thrombus formation.^{1,2,5} Also, despite the popularity of using

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LAD to define GLA, the left atrial volume index (LAVI) might be a better parameter in this regard.² The present study was carried out to determine the aetiology and clinical profile of GLA encountered over 8 years in a tertiary care cardiac hospital of a developing country.

Methods:

This was a single-centre, prospective, observational study carried out in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh, over 8 years from 2013 to 2021. The study protocol was approved by the Institutional Review Board of the Institute. Informed consent was taken from the participants. All patients diagnosed with GLA due to any cause over the above-mentioned period at NICVD were included in the study. GLA was defined as an LA having an anteroposterior diameter ≥ 80 mm in parasternal long axis (PLAX) view of conventional transthoracic echocardiography (TTE). In cases with repeated examinations, the initial one was selected.

Echocardiographic examination was carried out by the Vivid 7 and Vivid E95 echocardiography machine (GE Healthcare, 9900 Innovation Drive, Wauwatosa, WI 53226, USA). The examination was carried out as per the recommendation of the American Society of Echocardiography.^{8,9} LA volume was determined by Simpson's biplane method. LAVI was calculated by dividing the LA volume by the body surface area. The severity of valvular regurgitation and stenosis, as well as the mitral valve prolapse (MVP), were defined according to current guidelines.^{10,11} The end-point for follow-up comprised of all-cause death. The patient or the relatives were contacted over the phone.

Results:

Thirty cases of GLA were diagnosed over 8 years from 2013 to 2021 and included in the study. Out of 30 cases, 14 were male, and 16 were female. The mean age of the patients was 37.67 ± 11.22 years. The youngest patient was a 16-year-old female with MVP who presented with severe mitral regurgitation (MR). (Table 1) The oldest patient was a 59-year-old male who also had MVP with severe MR. (Table 1) The underlying aetiology was RHD in 22 cases, MVP in 7 cases, and flail anterior mitral leaflet (AML) in 1 case.

Among the RHD cases, isolated mitral stenosis (MS), isolated MR, mixed mitral valvular disease comprising of MS and MR, and multiple valvular disease comprising of mitral and aortic valvular disease were the underlying lesions in 3, 3, 7, and 9 cases, respectively. Among these patients, 1 had a history of percutaneous transvenous mitral commissurotomy (PTMC), 1 had a history of closed mitral commissurotomy (CMC), and 2 patients had mitral valve replacement (MVR). Out of 30 GLA cases, 16 had severe MR — 8 due to RHD, 7 due to MVP, and 1 due to flail AML. So, all MVP and the only flail AML cases presented with severe MR. Few patients with MVP were wrongly diagnosed as RHD for long before making the correct diagnosis. All cases presented with heart failure, on top of which 1 patient had dilated cardiomyopathy (DCM), and another 1 had an ischaemic stroke. None presented with Ortner's syndrome. ECG rhythm was analyzed in 28 cases; sinus rhythm was found in 3 patients only, permanent AF was present in 24 cases, and paroxysmal AF in 1 patient.

Echocardiography was done in all patients; however, some lack several parameters. Mean LAD was 92.13 ± 16.72 mm, ranging from 80 mm to 161 mm. The longest 161 mm LAD was found in a 52-year-old male patient with MVP and severe MR. LAVI was determined in 17 patients. The mean LAVI was 288.77 ± 134.40 ml/m², ranging from 161 ml/m² to 605 ml/m². The highest LAVI was found in a 35-year-old male patient having a history of MVR, severe MR, and moderate aortic regurgitation (AR). Mean pulmonary artery systolic pressure (PASP) was 64.5 ± 28.72 mmHg. Right ventricular (RV) function was recorded in all but 1 patient. RV dysfunction characterized by tricuspid annular plane systolic excursion (TAPSE) <16 mm, and/or or RV tissue Doppler systolic excursion velocity (RV S') <9.5 cm/sec was present in 19 patients. Out of 30 patients, LA thrombus was present in 5 patients, 6 had spontaneous echo contrast (SEC) in LA, 2 patients had both LA thrombus and SEC. During follow-up, 15 patients could not be contacted. The mean follow up duration was 0.99 ± 1.06 years, ranging from <1 month to 48 months. Out of 15 patients, 5 died, while 10 were alive. Mean survival was 1.8 ± 1.17 years, ranging from less than 1 year to 4 years.

Table-I
Clinical and echocardiographic profile of GLA patients (N=29)

Name, Age(Y), Sex, Date of first contact	Aetiology	ECG	LAD (mm)	LAVI ml/m ²	Thrombus, SEC	Comment
HA, 26, F 15.04.13	RHD, severe MS	AF	80	-	SEC	Died after 4 years
PB, 45, F 17.11.14	RHD, severe MS, mod MR, mod AS, mod AR	-	120	-	SEC and thrombus	Lost
TB, 55, F 15.06.15	RHD, severe MS	AF	103	-	Thrombus	Lost
HR, 29, M 20.02. 18	RHD; Severe MR, mod AS, mod AR	AF	109	-	SEC	Lost
MB, 50, F 23.03.18	RHD, severe MS, mod MR	AF	82	-	Thrombus	Died after 2 year
ZH, 52, M 16.08.18	MVP, severe MR	AF	161	-	None	Lost
SH, 38, M 12.01.19	RHD, post-MVR stenosis, mild MR	AF	84	-	None	Lost
MB, 33, M 27.01.19	RHD, mod MS, severe MR, severe AR	AF	80	214	None	Died after 1 year, post-DVR
RK, 26, F 04.02.19	MVP, severe MR	Sinus rhythm	87	269	None	Died after 1 year
MB, 52, F 22.04.19	RHD, severe MS, severe MR, mod AR	AF	80	207	None	Died after 1 year
SD, 55, M 08.06.19	RHD, severe MS	AF	86	-	SEC	Alive
SB, 30, M 12.06.19	RHD, severe MS, mod MR	AF	83	196	Thrombus	Lost
NB, 36, F 20.06.19	Flail AML, severe MR	AF	81	-	None	Lost
RB, 35, F	RHD, severe MR	AF	81	161	None	Alive
TK, 16, F 11.07.19	MVP, severe MR	Sinus rhythm	82	-	None	Lost
SB, 26, F 02.10.19	RHD, severe MR	-	89	-	None	Lost
BK, 24, M 11.11.19	MVP, severe MR	AF	82	254	None	Lost

(table continued)

Table-I (cont'd)

Name, Age(Y), Sex, Date of first contact	Aetiology	ECG	LAD (mm)	LAVI ml/m ²	Thrombus, SEC	Comment
SN, 50, F 22.02.20	RHD, severe MS, mod MR	AF	105	-	SEC	Lost
SK, 28, F 24.02.20	RHD, severe MS, severe MR, mild AR	AF	96	-	SEC	Lost
NI, 59, F 27.09.20	MVP, severe MR	AF	94	319	None	Alive
SM, 19, M 03.10.20	MVP, severe MR	AF	113	463	None	Lost
TZ, 35, M 21.11.20	Post-MVR severe MR, mod AR	AF	94	605	SEC	Lost
SH, 44, M 02.12.20	RHD, post-MVR, mild AR, DCM	AF	91	194	None	Alive
HB, 42, F 05.12.20	MVP, severe MR	Sinus rhythm	101	273	None	Lost
AK, 45, F08.12.20	RHD, post-CMC severe MS, severe MR, mild AS, mod AR	AF	82	224	Thrombus	Alive, recently had DVR
SY, 38, F 30.01.21	RHD, post-PTMC severe MS, severe MR	Paroxysmal AF	81	171	None	Alive
NB, 26, F 18.03.21	RHD, mod MS, severe MR, mild AS, mod AR	AF	81	221	None	Live
SH, 40, M 28.03.21	RHD, mod MS, severe MR, DCM	AF	81	183	Thrombus	Alive
MH, 41, M 20.04.21	RHD, severe MR	AF	91	584	None	Live, waiting for MVR
MA, 35, M 24.05.21	RHD, severe MS, severe MR, mid AR	AF	84	371	SEC and thrombus	Live, waiting for

MVR

GLA, giant left atrium; ECG, electrocardiography; LAD, left atrial diameter; LAVI, left atrial volume index; SEC, spontaneous echo contrast; RHD, rheumatic heart disease; MS, mitral stenosis; MR, mitral regurgitation; AS, aortic stenosis; AR, aortic

regurgitation; mod, moderate; MVP, mitral valve prolapse; AML, anterior mitral leaflet; DCM, dilated cardiomyopathy; PTMC, percutaneous transvenous mitral commissurotomy; MVR, mitral valve replacement; DVR, double valve replacement; AF, atrial fibrillation.

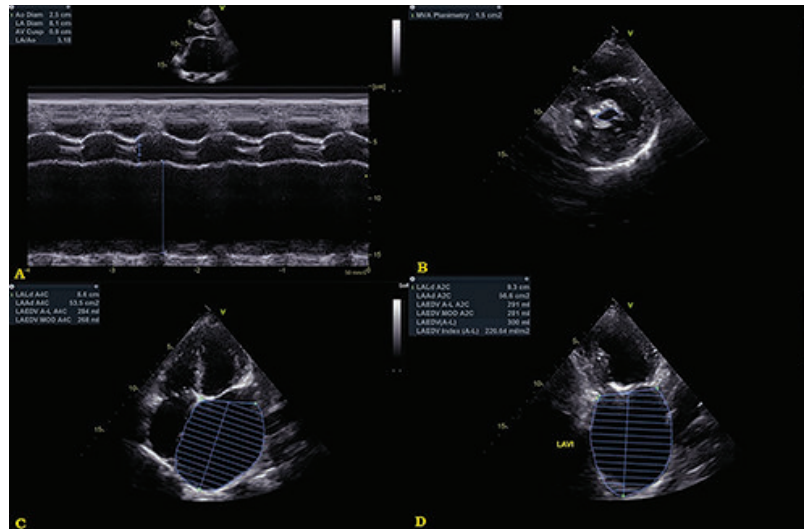


Fig.-1: Giant left atrium in a patient with rheumatic mitral valvular disease. Panel A, M-mode echocardiography showing dilated left atrium with left atrial diameter 81 mm. Panel B, 2D echocardiography left parasternal short axis view showing moderate mitral stenosis (yellow arrow) with mitral valve area 1.5 cm². Panel C and D, 2D echocardiography apical 4-chamber view showing left atrial volume index of 221 ml/m².

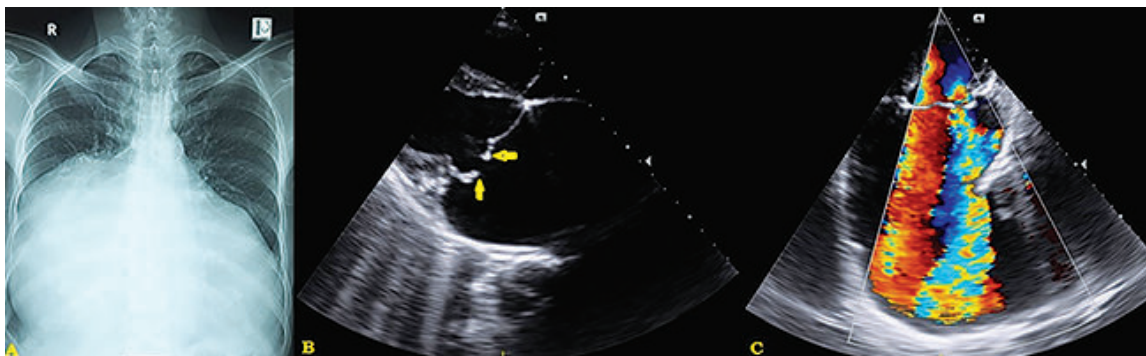


Fig.-2: Giant left atrium in a patient with mitral valve prolapse. Panel A, chest x-ray posteroanterior view showing huge cardiomegaly with the right cardiac border touching the right chest wall (black arrow). Panel B, 2D echocardiography left parasternal long-axis view showing prolapse of both leaflets of the mitral valve (yellow arrows) with non-coaptation (green arrow). Panel C, 2D-guided colour Doppler echocardiography apical 4-chamber view showing severe mitral regurgitation (green arrow).

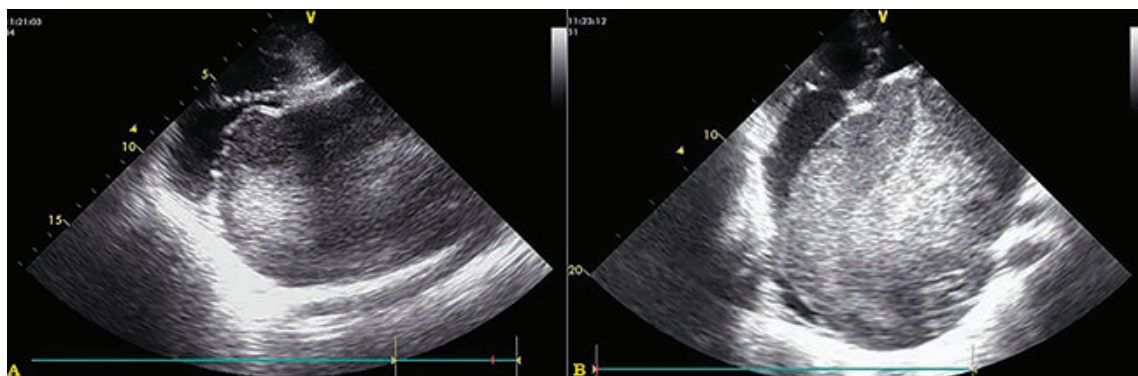


Fig.-3: Giant left atrium in a patient with isolated mitral stenosis. Panel A, 2D echocardiography left parasternal long-axis view showing features of severe mitral stenosis. Panel B, 2D echocardiography apical 4-chamber view showing hugely dilated left atrium. Both panels A and B show dense spontaneous echo contrast in the left atrial cavity, hiding accompanying thrombus which was extracted per-operatively.

Discussion:

Definition of GLA lacks a uniform consensus.^{2,4} In the present study, GLA was defined as any LA having a diameter of ≥ 80 mm in PLAX view of conventional TTE. Before the advent of medical imaging, ‘extreme dilatation of the left auricle’ was described by Owen and Fenton in 1901 clinically by the presence of dullness on percussion on the right chest in a 40-year-old lady with a history of rheumatic fever and subsequent post-mortem examination.¹² Subsequently, a chest x-ray was used rather than the clinical method only; GLA was defined as an LA which “touched the right chest wall or extended within one centimetre of it on a posteroanterior chest x-ray.”⁵ Cardiothoracic ratio (CTR) ≥ 0.7 was also used as a criterion for GLA.¹³ In the 1960s, echocardiography was introduced and became the imaging modality of choice for diagnosing GLA. LAD ≥ 80 mm in TTE with CTR ≥ 0.7 in CXR was the criterion used to define GLA by Piccoli et al.¹⁴ Even less stringent measure of LAD ≥ 65 mm in TTE had been used in this regard.¹⁵ LA is a 3-dimensional structure, and measurement of LAD may not be the optimum parameter to assess the enlarged LA. Here, measurement of volume rather than diameter may be a better way to study and define GLA.^{1,2} In this study, LAVI was determined in 17 out of 30 cases. Unfortunately, no criteria to define GLA based on LAVI are available to date. The mean LAVI was 288.77 ± 134.40 ml/m² in the present study. The mean LAD was 89 mm (range 80 - 121 mm), and the mean LA volume (not volume index) was 593.96 ml (range 364.3 ml to 921 ml) in the study by El Maghraby and Hajar.² On the other hand, the median LAD was 67 mm (range 66–71 mm), and the median LAVI was 118.9 mL/m² (range 100.2–149.1 mL/m²) in a Korean study.¹ Noteworthy that the former study used the criterion of LAD ≥ 80 mm to define GLA like the present study, whereas the latter study used the cut-off point of 65 mm to define GLA. In the present study, mean LAD was 92 mm, and mean LAVI was 289 ml/m²; taken these values, for 80 mm cut-off of LAD, corresponding LAVI is 251 ml/m². Whether this cut-off value of LAVI of ~ 250 ml/m² can be used to define GLA needs further study.

Consistent with the previous case reports, case series, and studies, the predominant cause of GLA

in the present study was RHD, responsible for almost 3/4^{ths} of 30 cases. However, it is noteworthy that the resting 1/4th cases, i.e., 8 were due to non-rheumatic causes (MVP, flail AML). Historically, since 1901, almost all cases of GLA reported were due to RHD. The series of 10 cases of GLA described by DeSanctis et al. in 1964 from the Massachusetts General Hospital, the USA, over 30 years were all due to the RHD. Also, during that time, like ours now, RHD was not uncommon in the Western world, including the USA. However, the situation has changed, and RHD is now rare there. GLA is at present only rarely reported in the USA and is mostly involving immigrants.¹⁶ On the other hand, despite the transition in disease epidemiology, RHD is still prevalent in developing countries, including Bangladesh.¹⁷ So, logically, RHD would continue to be the dominating cause of GLA in these parts of the world. RHD was the underlying condition in the majority of cases of GLA in more recent studies; however, other causes like MVP, functional MR, hypertrophic cardiomyopathy and cardiac amyloidosis have also been identified as significant or rare causes.^{1,2,18-21} With further control of rheumatic fever and RHD, MVP may top the otherwise small list of aetiological diagnoses of GLA in the future.

Analysis of the pattern of valvular lesions causing GLA due to RHD, MR was the dominant lesion over MS in the majority. This observation is consistent with those of previous studies.^{2,5,13} Isolated MS as a cause of GLA was described only rarely in the past.¹³ Out of 38 cases of GLA referred for mitral valve surgery, isolated MS was found in 29%, MR in 21%, combined MS and MR in 50%, and aortic pathology was associated in 45%.¹³ In the present study, 3 out of 30 (i.e., 10%) cases were due to isolated MS.

Out of 30 patients, LA thrombus was present in 5 patients, 6 had SEC in LA, 2 patients had both LA thrombus and SEC. Despite the massive LA and the common association of AF, thrombus formation is relatively infrequent in GLA.⁵ The underlying reason behind this apparent paradox is severe MR which tends to prevent stasis. In the present study, 43% of the cases had either thrombus or SEC in LA, and the latter is generally considered as the precursor of the former.²²

Presence of a fair number of cases of MS may be the explanation of the more common occurrence of thrombus and SEC in the present series. Strikingly, embolism was relatively uncommon – only 1 patient presented with ischaemic stroke. Thromboembolism was also rarely described in previous reports.^{2,5}

In the present study, follow-up was done mainly via telephone. Adequate information was available for 15 cases only. The mean duration of follow up was 11.88 months, ranging from <1 month to 48 months. Out of 15 patients, 5 died, and 10 were alive. One patient died within 1 week of double valve replacement (DVR), while 1 patient recently had DVR. Some of the GLA cases could not be contracted because of incomplete records or lack of response to the recorded phone number. This is the real-world situation, presumably in many developing countries. Despite incomplete follow-up, some observations can be made. Most of the patients did not receive surgical treatment; instead, they were managed medically. Poverty, inadequate facilities for surgical treatment, presence of high-risk features, and tendency to adopt less aggressive treatment strategy by the cardiac surgeons may be responsible.

The study has got some critical limitations. The follow-up was suboptimal. Out of 30 patients, only half could be traced. The underlying cause of death could not be ascertained in every case. Also, LAVI was not determined in all cases. The strength of this study is that it includes the all-comer real-world patients with an otherwise rare clinical entity. It may be one of the most extensive series of GLA cases with such stringent definition of GLA of ≥ 80 mm reported so far. Also, some observations and recommendations have been made regarding the use of LAVI to define GLA in place of LAD, though they need further confirmation.

Conclusion:

GLA is a rare and rather heterogeneous entity. Physicians should have appropriate preparedness to deal with GLA in the present century. More information regarding GLA based on advanced imaging modalities like 3-dimensional echocardiography, cardiac computed tomography and cardiac magnetic resonance may be warranted.

What is Already Known?

- Giant left atrium (GLA) is commonly defined using chest x-ray or transthoracic echocardiography.
- Cardiothoracic ratio (CTR) of ≥ 0.7 in chest x-ray postero-anterior view defines the GLA.
- Echocardiographically, GLA is defined variably as the LA diameter ≥ 65 mm or ≥ 80 mm.
- Rheumatic mitral valvular disease is known to be the commonest aetiology.
- Mitral valve replacement is associated with variable outcome.

What this Study Adds?

- Left atrial volume index (LAVI) determined by echocardiography may be a better alternative for definition of GLA
- LAVI of ≥ 250 ml/m² for defining GLA needs further study.
- Rheumatic mitral valvular disease continues to be the dominant cause of GLA.
- Mitral valve prolapse may be increasingly important contributor of GLA
- Management of GLA in these parts of the world may need further optimization.

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