A Dissertation on

ASSESSMENT OF PROTHROMBOTIC BURDEN IN PATIENTS WITH RHEUMATIC HEART DISEASE USING PLASMA D-DIMER ASSAY

PLACE: DEPARTMENT OF CARDIOLOGY

Submitted to

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY CHENNAI

In partial fulfillment of the regulations

for the award of the degree

D .M. CARDIOLOGY

GOVT. STANLEY MEDICAL COLLEGE HOSPITAL

CHENNAI – TAMIL NADU

AUGUST-2012

CERTIFICATE

This is to certify that this dissertation entitled **"ASSESSMENT OF PROTHROMBOTIC BURDEN IN PATIENTS WITH RHEUMATIC HEART DISEASE USING PLASMA D-DIMER ASSAY"** Submitted by Dr. P. SAMPTH KUMAR., to the Tamil Nadu Dr. MGR Medical University is in partial fulfillment of the requirement for the award of D.M. CARDIOLOGY DEGREE and is a bonafide research work carried out by him under direct supervision and guidance.

Signature of the Professor and HOD

DR . G. RAVI SHANKAR MD.DM.,

Signature of The DEAN

DR .S. GEETHALAKSHMI., M.D., Ph.D.,

DECLARATION

I solemnly declare that the dissertation entitled **"ASSESSMENT OF PROTHROMBOTIC BURDEN IN PATIENTS WITH RHEUMATIC HEART DISEASE USING PLASMA D-DIMER ASSAY"** Was done by me at the Government Stanley Medical college Hospital during 2010-2012 under the guidance and supervision of PROFESSOR DR G.RAVI SHANKAR MD.DM., The dissertation is submitted to the Tamil Nadu DR. MGR Medical University towards the partial fulfillment of the requirements for the award of D.M(CARDIOLOGY)

Place: Chennai

Date : 12/3/2012 Dr. P. SAMPTH KUMAR..

ACKNOWLEDGEMENT

I owe my thanks to the Dean, Government Stanley Medical College and Hospital, Professor **Dr. S. GEETHALAKSHMI MD., Ph.D**., for allowing me to avail the facilities needed for my dissertation work.

I am extremely grateful to the Professor and Head of the Department of Cardiology, Government Stanley Medical College and Hospital. **DR.G. RAVI SHANKAR MD., DM.,** for permitting me to do the study and for being a constant source of encouragement.

My heartfelt gratitude to my unit Additional Chief **DR.A.S. ARUL MD DM.,** professor of Cardiology Government Stanley Medical College and Hospital for the wholesome support and valuable guidance without which I would not have completed this study.

I am extremely grateful to my unit assistant professors **DR.M.NANDHAKUMAR MD.,DM., DR.ASHOKVICTOR MD.,DM, DR. P.M.NAGASWARN MD., DM., DR. K.TAMILSELVAN MD., DM., DR.C.ELAMARAN MD.,DM.,** & to my co - PG DR. G. MANOGAR for their valuable suggestions and support.

CONTENTS

ABBREVIATIONS AND ACRONYMS

RHD - RHEUMATIC HEART DISEASE

MS - MITRAL STENOSIS

MR - MITRAL REGURGITATION

SR - SINUS RHYTHM

AF - ATRIAL FIBRILLATION

AS - AORTIC STENOSIS

AR - AORTIC REGURGITATION

LAA - LEFT ATRIAL APPENDAGE

TTE - TRANS THORACIC ECHOCARDIOLOGY

MVA - MITRAL VALVE AREA.

LA - LEFT ATRIUM

INTRODUCTION

In spite of tremendous and advanced improvement both in preventive aspects as well as therapeutic part Rheumatic Heart Disease forms a part of health hazard in developing countries. A part of complication of RHD puts these patients for a major morbidity leading to mortality. So this preventable complication i.e. thromboembolic manifestation to a extent can be predicted, and it is taken as my study.

This study based on plasma D-dimer levels and predicting a major adverse event, thromboembolic manifestation in these patients. Plasma D-dimers are cross linked fibrin derivatives which result from degradation of fibrin by endogenous fibrinolytic system.

They reflect both increased coagulation and an active fibrinolytic system and are markers for clot risk.

AIMS AND OBJECTIVES

Assessing prothrombotic burden in patients with Rheumatic heart diseases with AF or without AF using plasma D-dimer levels and comparing the D-dimer levels among the Rheumatic heart disease patients with various subsets of patients.

Correlation of AF to left atrial size and to age and to D-dimer level in the study sample.

Correlation of mitral regurgitation to D-dimer level as a part of systemic hypo fibrinolytic state.

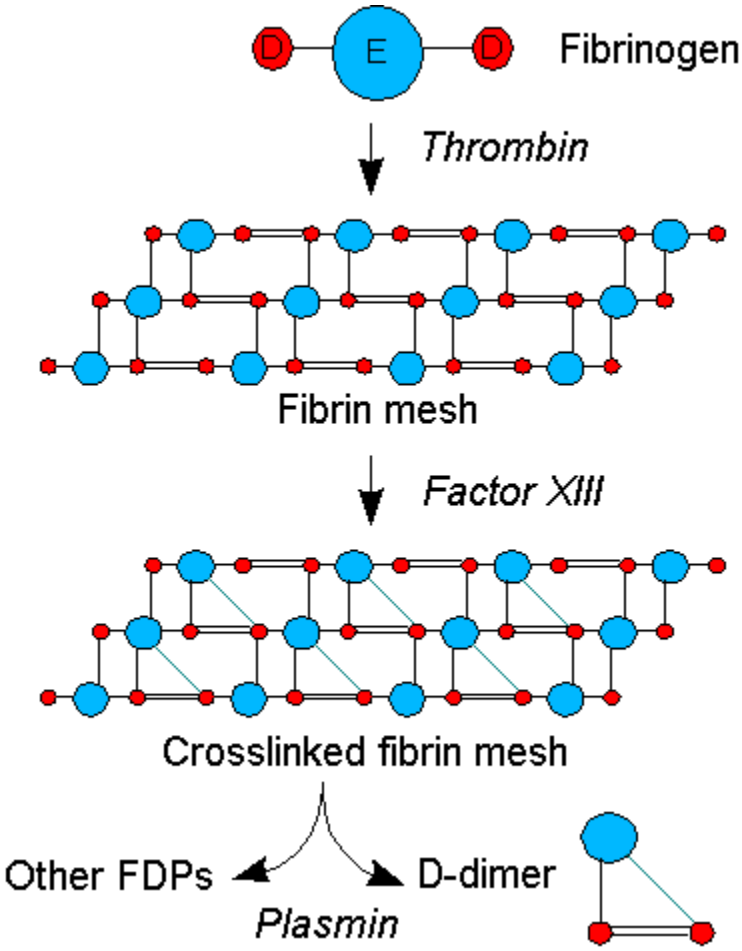
Correlating left atrial empting velocity to D-dimer level as a part of Intra atrial hemodynamics.

REVIEW OF LITERATURE

Plasma D-dimers

Plasma D-dimers are cross linked fibrin derivatives which result from the degradation of fibrin by the endogenous fibrinlytic system(1). They reflect both increased systemic coagulation and an active fibrinolytic system, and are markers for thromboembolic risk(2,3,4)**.** D-dimer is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two crosslinked D fragments of the fibrinogen protein.

D-dimer concentration may be determined by a blood test to help in diagnosing thrombosis. Since its introduction in the 1990s, it has become an important test performed in patients suspected of thrombotic disorders. While a negative result practically rules out thrombosis, a positive result can indicate thrombosis but does not rule out other potential causes. Its main use, therefore, is to exclude thromboembolic disease where the probability is low. In addition, it is used in the diagnosis of the blood disorder, disseminated intravascular coagulation.



Coagulation, the formation of a blood clot or thrombus, occurs when the proteins of the "coagulation cascade" are activated, either by contact with damaged blood vessel wall (intrinsic pathway) or by activation offactor VII by tissue activating factors. Both pathways lead to the generation of thrombin, an enzyme that turns the soluble blood protein fibrinogen into fibrin, which aggregates into proteofibrils. Another thrombin-generated enzyme, factor XIII, then crosslinks the fibrin proteofibrils at the D fragment site, leading to the formation of an insoluble gel which serves as a scaffold for blood clot formation.

The circulating enzyme plasmin, the main enzyme of fibrinolysis, cleaves the fibrin gel in a number of places. The resultant fragments, "high molecular weight polymers", are digested several times more by plasmin to lead to intermediate and then to small polymers (fibrin degradation products or FDPs). The cross-link between two D fragments remains intact, however, and these are exposed on the surface when the fibrin fragments are sufficiently digested. The typical D-dimer containing fragment contains two D domains and one E domain of the original fibrinogen molecule.

D-dimers are not normally present in human blood plasma, except when the coagulation system has been activated, for instance because of the presence of thrombosis or disseminated intravascular coagulation. The D-dimer assay depends on the binding of a monoclonal antibody to a particular epitope on the D-dimer fragment. Several detection kits are commercially available; all of them rely on a different monoclonal antibody against D-dimer. Of some of these it is known to which area on the D-dimer the antibody binds. The binding of the antibody is then measured quantitatively by one of various laboratory methods.

D-dimer testing is of clinical use when there is a suspicion of deep venous thrombosis (DVT), pulmonary embolism (PE) or disseminated

intravascular coagulation (DIC). It can also rise postoperatively. It is under investigation in the diagnosis of aortic dissection.

For DVT and PE, there are various scoring systems that are used to determine the clinical probability of these diseases; the best-known were introduced by Wells et al For a very high score, or pretest probability, a D-dimer will make little difference and anticoagulant therapy will be initiated regardless of test results, and additional testing for DVT or pulmonary embolism may be performed.

`For a moderate or low score, or pretest probability:

A negative D-dimer test will virtually rule out thromboembolism: the degree to which the D-dimer reduces the probability of thrombotic disease is dependent on the test properties of the specific test used in the clinical setting: most available D-dimer tests with a negative result will reduce the probability of thromboembolic disease to less than 1% if the pretest probability is less than 15-20%

If the D-dimer reads high, then further testing (ultrasound of the leg veins or lung scintigraphy or CT scanning) is required to confirm the presence of thrombus. Anticoagulant therapy may be started at this point or withheld until further tests confirm the diagnosis, depending on the clinical situation.

In some hospitals, they are measured by laboratories after a form is completed showing the probability score and only if the probability score is low or intermediate. This would reduce the need for unnecessary tests in those who are high-probability.

Various kits have a 93-95% sensitivity and about 50% specificity in the diagnosis of thrombotic disease.

1) False positive readings can be due to various causes: liver disease, high rheumatoid
   factor, inflammation, malignancy, trauma, pregnancy,
   recent surgery as well as advanced age
2) False negative readings can occur if the sample is taken either too early after thrombus formation or if testing is delayed for several days. Additionally, the presence of anti-coagulation can render the test negative because it prevents thrombus extension.
3) Likelihood ratios are derived from sensitivity and specificity to adjust pretest probability.
4) D-dimer was originally described in the 1970s, and found its diagnostic application in the 1990s.

ATRIAL FIBRILLATION AND MITRAL STENOSIS

Atrial fibrillation (AF) and mitral stenosis (MS) especially in combination, increase the risk of left atrial thrombus formation and systemic embolization(5). Both, AF and MS cause the stagnation of blood in the left atrium, which in turn causes rouleaux formation of the red blood cells that is observed as echocardiographic "spontaneous echo contrast" and intracardiac thrombosis(6,7,8,9,10,11,12) . The blood flow and endoluminal shear stresses presumably must be below a critical value in order to form intra cardiac SEC and thrombus formation to occur.

Atrial fibrillation (AF) is the most common sustained arrhythmia in the world, occurring in approximately 0.4% of the general population. The prevalence of AF increases with age, affecting upto 5% of the population over the age of 69 years.

AF is most commonly associated with advanced age, hypertension, valvular heart disease, congestive cardiac failure and coronary artery disease. It has also been associated with physiological stress, drugs, pulmonary embolism, chronic lung disease, hyperthyroidism, caffeine, infections and various metabolic disturbances. Other less common

cardiac associations include Wolf-Parkinsonism White syndrome. Pericarditis and cardiomyopathy.

AF due to progressive dilation of the left atrium in mitral stenosis is very common; its onset precipitates pulmonary edema. Less than 20% of the patients remain in sinus rhythm, which is often associated with a small fibrotic left atrium and severe pulmonary hypertension. All patients are predisposed to left atrial thrombus and systemic thromboembolism previously account for 25% of all deaths in this condition, when anticoagulation therapy had not been available.

Plasma D-dimers are cross-linked fibrin derivatives which result from the degradation of fibrin by the endogenous fibrinolytic system. They reflect both increased systemic coagulation (thrombogenesis) and an active fibrinolytic system, and are markers for thromboembolic risk.

LEFT ATRIUM

The LA fulfills 3 major physiologic roles that impact on LV filling and performance. The LA acts as a contractile pump that delivers 15% to 30% of the LV filling, as a reservoir that collects pulmonary venous return during ventricular systole, and as a conduit for the passage of stored blood from the LA to the LV during early ventricular diastole. Increased LA size is associated with adverse cardiovascular outcomes.

An increase in atrial size most commonly is related to increase wall tension as a result of increased filling pressure. Although increased filling volumes can cause an increase in LA size, the adverse outcomes associated with increased dimension and volumes are more strongly associated with increased filling pressure. Relationships exist between increased LA size and the incidence of atrial fibrillation and stroke. LA enlargement is a marker of both the severity and chronicity of diastolic dysfunction and magnitude of LA pressure elevation. The LA size is measured at the end-ventricular systole when the LA chamber is at its greatest dimension.

LA LINEAR DIMENSION

The LA can be visualized from multiple echocardiographic views from which several potential LA dimensions can be measured. However, the large volume of prior clinical and research work used with M-mode or 2D anterio- posterior (AP) linear dimension obtained from the parasternal long axis view, making this as standard for linear LA measurement. The convention for M-mode measurement is to measure from the leading edge of the posterior aortic wall to the leading edge of the posterior LA wall. However, to avoid the variable extent of space between the LA and aortic root, the trailing edge of the posterior aortic wall is recommended.

LAA FLOW IN ATRIAL FIBRILLATION

Active LAA flow is commonly observed in patients with AF with alternating positive and negative sawtooth-appearing flow signals of variable amplitude and regularity. Mean LAA flow velocities have greater physiologic significance than peak velocities. These should be averaged for each cardiac cycle and then averaged for several cycles. Generally, flow velocities during AF are lower than those during sinus rhythm. However, flow velocities in patients with AF are highly variable,

with high velocity flows on one end of the spectrum (velocities similar to or even exceeding, those observed in sinus rhythm,) and minimal to absent flow on the other end. This represents the wide continuum of LAA contractile contraction to complete paralysis of the appendage. Of mitral and Aortic valve disorders, rheumatic mitral stenosis is most commonly associated with thromboembolism, irrespective of co-existence of MR. AF increase the risk thromboembolism upto 18 times, thrombi associated with MS can be found on either the atrial wall or in its appendage. The Risk of thromboembolism in rheumatic valve stenosis is related to age and low cardiac output, yet it does not correlate well with left atrial size, mitral calcification or severity of mitral stenosis. The Association of MR with thromboembolism correlates with the co-existence of MS.

ROLE OF DRUGS

Oral anticoagulant reduces risk of stroke in patients with rheumatic mitral stenosis particularly those with co-existent atrial fibrillation. Pre risk – benefit ratio in those without AF is not known. The Benefit of

antiplatelet agents in the prevention of stroke in patients with any type of Rheumatic valvular disease has not established. Of those patients who have had one events, early Recurrent embolism has been reported in upto two thirds and aggressive anticoagulation instituted.

MITRAL VALVE DISEASE AND LAA FLOW

Hemodynamically significant mitral stenosis increase the resistance to both active and passive LAA emptying, resulting in an overall lowering of LAA flow regardless of the specific rhythm. Hwang et al(13). Have demonstrated a marked decrease in LAA contraction velocities in patients with mitral stenosis, compared with patients without rheumatic heart disease, both in sinus rhythm and in AF. In addition to overall important of LAA function, mitral stenosis specifically limits the normal augmentation of LAA flow during diastole in patient with AF, a phenomenon related to the severity of the stenosis. In the presence of AF, patients with severe mitral stenosis typically demonstrate low-to-absent LAA velocities. This is in contrast to nonrhemuatic AF, which is associated with a wide spectrum of flow velocities, with both “high

velocity". These effects of mitral stenosis on LAA function are probably the result of the severe hemodynamic impairment in patients with mitral stenosis. Direct LA and LAA involvement in the rheumatic inflammatory process, and an atrial myopathy resulting from chronic LA pressure elevation, are additional possibilities. Hemodynamically significant mitral regurgitation is predicted to impair LAA function via LA and LAA dilatation and increased filling pressure. Despite a possible deleterious effect of mitral regurgitation on LAA function, mitral regurgitation has an overall protective effect against thromboembolism by prevention of LA stasis.

Many studies have suggested that determination of LAA function by echocardiography allows the identification of patients with AF or AFL who are at high risk for the development of LA or LAA thrombi and thromboembolic complications.

Cardiogenic embolism accounts for ≥15% of ischemic strokes. Left atrial appendage (LAA) thrombi are believed for be the source of embolic in a substantial number of these patient, primarily in association

with atrial fibrillation (AF) or rheumatic mitral valve disease. Despite the blind cul-de-sac and multiple anatomic structure of the LAA, thrombus formation is normally prevented by vigorous blood flow in the appendage cavity. Nevertheless, LAA dysfunction in various pathophysiologic state may predispose to local thrombosis and systemic embolization.

PATHOPHYSIOLOGY OF LAA FUNCTION

Age-associated changes in LAA velocities have been described. Aging was associated with a progressive linear decline in all LAA flow variables (LAA contraction and filling velocities and early diastolic LAA flow). A possible effect of various systemic diseases (e.g., hypertension) on LAA function has not been determined.

ECHOCARDIOGRAPHIC CORRELATES.

1) LA/LAA size: in patients with sinus rhythm, there is no clear association between LA size and LAA flow velocities (15). However, concomitant LAA enlargement and low LAA contraction velocities are common in patients with mitral stenosis who are in sinus rhythm. In

patients with AF, larger LA and LAA sizes commonly are associated with lower LAA flow velocities(16,17,18), both in patients with and in those without associated rheumatic mitral disease. This is most pronounced in patients with near absence of LAA flow, in whom significant dilation of the LA and LAA is the rule. Of note, significant LAA dilation resulting from any cause may potentially further impair LAA function by increasing LAA wall stress.

2) LAA flow versus mitral and pulmonary venous flow:

The following correlations were observed between LAA flow velocities and mitral inflow and pulmonary venous flow velocities in the presence of sinus rhythm:

a) Lack of correlation (19) or even a negative correlation between LAA contraction velocities and mitral inflow A velocities,

b) Lack of correlation between LAA and pulmonary venous flow velocities, and

c) Significant positive

Correlation between early diastolic LAA outflow and both mitral E velocities and pulmonary venous diastolic velocities, all of which decline progressively with aging due to age-related slowing of LV relaxation.

LAA function versus global LA function.

Various methods developed to evaluate LA contractile function are time-consuming and, thus, not routinely used in clinical practice. Hence, it is tempting to apply LAA flow variables as clinically applicable surrogates for global LA function(20,21), although the validity of such an approach is questionable. The LAA and main LA cavity are derived embryologically from different sources. The trabecular LAA is a remnant of the embryonic LA, whereas the smooth LA cavity is derived from an outgrowth of the pulmonary veins. Therefore, it is conceivable that LAA function may dissociate from global LA function. The following arguments support this:

1) Dissociation of LAA and LA function has been anecdotally reported during sinus rhythm in patients with preserved global LA function (manifested as normal mitral inflow A velocities), but low or absent LAA

flow velocities, in association with LAA thrombus formation, spontaneous echocardiographic contrast and clinical embolic events.

2) Dissociation of LA and LAA mechanical activity has been described recently in patients after cardioversion, in whom organized LA mechanical activity may be present along with disorganized LAA contraction.

LAA FUNCTION BY DOPPELER

The LAA has been imaged primarily by transthoracic echocardiography (parasternal short-axis view of the base of the heart or apical two chamber view).

1) LAA view- The view with the optimal alignment of Doppler with LAA flow, as determined by colour flow imaging, should be selected. No differences in Doppler velocities have been noted using various LAA views (22, 23).

2) Sample volume location-Currently, there is no standard sampling site in the appendage (i.e., sampling at the LAA-LA junction versus sampling at different sites within the LAA cavity). It is unclear whether variations in sampling site location produce significant changes in measured

velocities, as demonstrated for other Doppler measurements such as mitral inflow velocities (24). In a recent report, a small trend was observed for lower velocities at the wider orifice of the LAA, in comparison with velocities obtained at the narrower middle portion of the appendage (25). LAA flow should be sampled at the site of maximal flow velocities (determined by color flow imaging), while avoiding wall motion Doppler artifacts, which are commonly observed in the more distal (narrow) portions of the appendage. In practice, technically adequate tracings of maximal LAA flow velocities are commonly recorded within the proximal third of the appendage.

3) Doppler sample size and machine gains-These are set to visualize a spectral Doppler signal with a clear envelope, typical of the normal laminar appendage flow. Initially, filters are set at low values to enable visualization of low velocity flow, characteristic of early diastolic LAA flow in sinus rhythm and LAA flow in a subset of patients with AF.

METHODOLOGY

PATIENTS

The study population included ’65’ patients who are consecutive samples coming to our OPD and patients who are admitted in our ward. Rheumatic mitral valve disease was diagnosed by the presence of any senotic & regurgitation seen in at least two planes by Doppler echocardiography, and accompanied by at least two of the following three morphological abnormalities of the regurgitant valve: restricted leaflet mobility; focal or generalized valvular thickening; and abnormal subvalvular thickening. In order to provide a definite diagnosis of rheumatic heart disease, these features had to be identified concordantly by each of the echocardiographers, all of whom were experienced in the diagnosis and treatment of rheumatic heart disease

Exclusion criteria

1) Patients aged > 60 years,

2) With any history of surgery

3) Acute coronary syndrome during the past 12 weeks

4) On anticoagulation medications

5) Also who had a history of stroke

6) Systemic thromboembolism,

7) Deep venous throumbus,

8) Intracardiac thrombus on transthoracic echocardiography,

9) Uncontrolled hypertension,

10) Left ventricular systolic failure with ejection fraction < 40%,

11) Any disease related to and acute phase reaction (acute infection, malignancy, end-stage liver disease or chronic renal failure (creatinine clearance <35 ml/min or diabetes) were excluded from the study.

12) Any subjects with a recent history of trauma or surgery were also excluded.

13) Those patients receiving aspirin stopped their medication five days before venous blood samples were obtained.

14) Patients in chronic AF were not receiving warfarin secondary to any contraindication, non-compliance or personal preference.

15) Patients with non-rheumatic causes of MR were not enrolled into the study.

All patients provided their informed consent to participate in the study, which was approved by the institutional ethical committee.

INCLUSION CRITERIA:

1. All patients with RHD with mitral valve and aortic valve disease.
2. Age less than 60 yrs.
3. Rheumatic heart disease patients in sinus rhythm and in Atrial fibrillation.

Echocardiographic examinations

Transthoracic echocardiography examinations were performed using a 3.5mHz sector transducer with Esaote my lab 5000 echocardiography system. The mitral valve area (MVA) was calculated using planimetry and pressure half –time methods; MS was defined as Mild, Moderate, Severe, by both method. Mitral regurgitation was classified as mild MR (jet area <4 cm^2), moderate (2D MR jet area 4-8cm^2) or severe (2D MR jet area >8 cm^2). Eccentric MR jets were

classified as severe when a pulmonary venous systolic reverse flow was detected with Doppler examination. All echocardiographic examinations done using TTE with patients in the left lateral decubitus position with esaote system. The transducer was placed somewhat superior and outside from the position viewing conventional parasternal short axis image of the aortic valve, angle between LA appendage midline and Doppler beam narrowed. The LAA was carefully sought and visualized on the left side of the aorta and on the right inferior side of main pulmonary trunk. The left atrial appendage flow velocity was recorded by pulsed Doppler Echocardiography with sampling volume placed at the left atrial appendage orifice

Sample Collection.

Blood samples were obtained between 7:00 and 9:00am, after an overnight fast and at least a 20-min rest period, from the antecubital vein of the patients. Samples were transported to the laboratory at room temperature within 45 min after venipuncture. Sodium citrate solution (0.2ml) was mixed with 1.8ml of venous blood and centrifuged for 10min

at 3,500 r.p.m. The plasma (as supernatant) was removed at + 15C, and the results were measured using a commercial particle enhanced immunoturbidimetry. The intra – and inter- assay coefficients variation were less than 4%. Normal plasma levels of D-dimer range from 0 to 0.4 µgm FEU/ml

Statistical Analysis

All statistical analyses were conducted using SPSS version 16.0 for windows. The results were analyzed with descriptive statistical methods (mean±SD), as the D- dimer levels were found to be normally distributed . The numbers were rounded to the nearest integral for data presentation. Differences between groups were analyzed using student t test to analyse and compare two means, descriptive data were used for chi-square analysis. And significant differences were found between the subgroups. A p-value <0.05 was considered to be statistically significant.

RESULTS AND ANALYSIS

The mean age of the 65 study patients was 34± 10.

And Atrial fibrillation was present in 17% of the study population. The samples are subdivided into various sub groups based on the patients heart rhythm and valvular pathology.

The highest D-dimer levels were present in the MS +MR+ AF subgroup, lowest levels of are found in MR+ SR subgroup

Males comprised 26 (40%) and female 39 (60%) of the total. Majority 54 (83.08 %) of the sample were NSR and 11 (16.92 %) were in AF. The distribution between Gender and AF were not differed statistically.

Majority among females 33 (84.62%) of them having MS while comparing males 15 (57.69 %). The distribution between Gender and MS differed statistically ($P < 0.02$).

Table-1

Age distribution of the Sample

Age Group	Male		Female		Total	
	No of Patient	**%**	**No of Patients**	**%**	**No of Patients**	**%**
< 20	3	11.54	2	5.13	5	7.69
21- 30	10	38.46	15	38.46	25	38.46
31 -40	6	23.08	8	20.51	14	21.54
41–50	7	26.92	13	33.33	20	30.77
51-60	0	0	1	2.56	1	1.54
Total	26	100	39	100	65	100
Mean ± Sd	**32.19 ± 9.30**		**35.05 ± 10.25**		**33.91 ± 9.91**	
	t=1.14 df=63 Not Significant					

Patients were distributed across the age spectrum of 14 to 54 years.

Mean age of the patients was **33.91 ± 9.91 (male 32.19 ± 9.30** and female **35.05 ± 10.25)** years. Most patients (n=25) were in the age group of 21-30 years. Youngest patient was 14 years old.

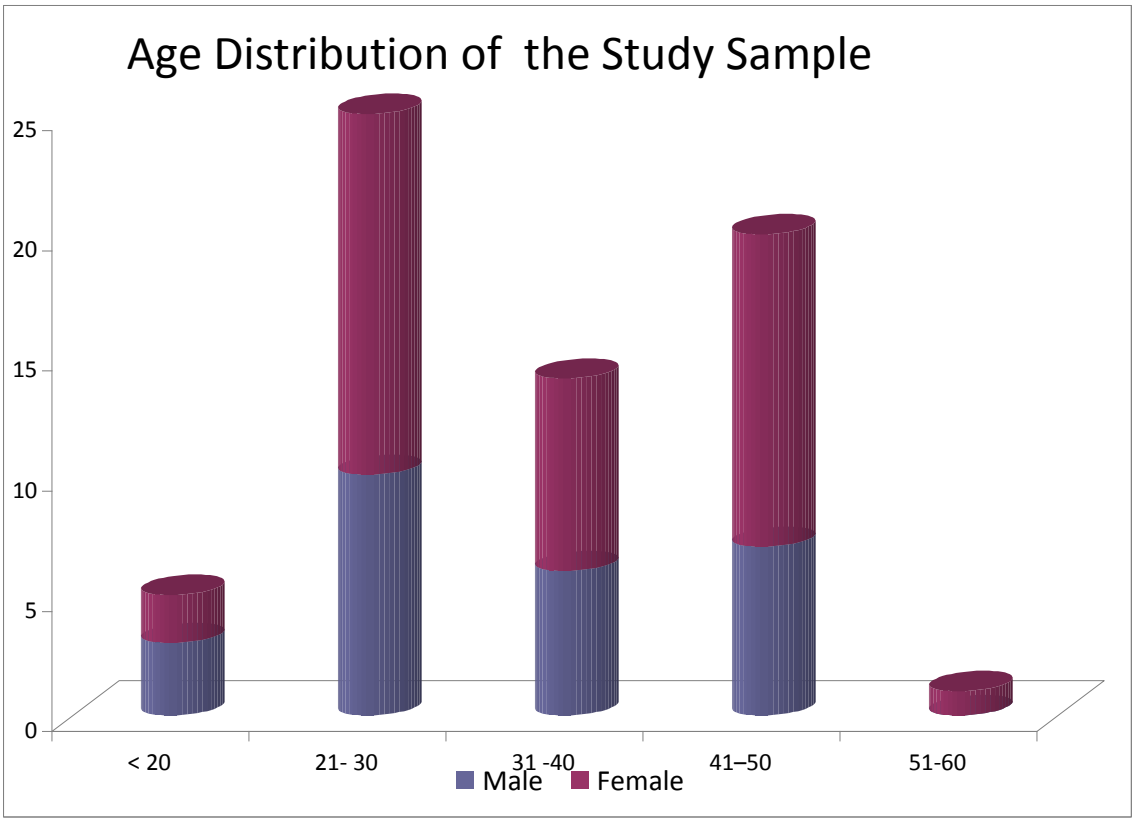

Age Distribution of the Study Sample
25
20
15
10
5
0
< 20
21- 30
31 -40
41–50
51-60
Male
Female

Table-2

Weight & Height

	Male	**Female**	**Total**	**Significant**
	Mean ± sd	**Mean ± sd**	**Mean ± sd**	(Male Vs Female)
Weight (Kg)	56.42 ± 7.40	51.90 ± 8.18	53.71 ± 8.13	t=2.27 df=63 P<0.03
Height (Cm)	160.15 ± 3.48	153.31 ± 6.37	156.05 ± 6.34	t=5.00 df=63 P<0.0001

Sd= Standard Deviation NS – Not Significant

The above table reveals that males had high Weight (male 56.42 ± 7.40), female (51.90 ± 8.18) and Height (male 160.15 ± 3.48 and female 153.31 ± 6.37) than females. The t-value reveals that there is significant association between Weight (P<0.03) with Gender and Significant association between Gender with Height (P<0.0001)

Table-3

ATRIAL FIBRILATION

	Male		**Female**		**Total**	
	No of Patient	**%**	**No of Patients**	**%**	**No of Patients**	**%**
AF	5	19.23	6	15.38	11	16.92
NSR	21	80.77	33	84.62	54	83.08
Total	**26**	**100**	**39**	**100**	**65**	**100**
	Chi square =1.16 df=1 NS					

Males comprised 26 (40%) and female 39 (60%) of the total. Majority 54 (83.08 %) of the sample were NSR and 11 (16.92 %) were AF. The distribution between Gender and ECG were not differed statistically.

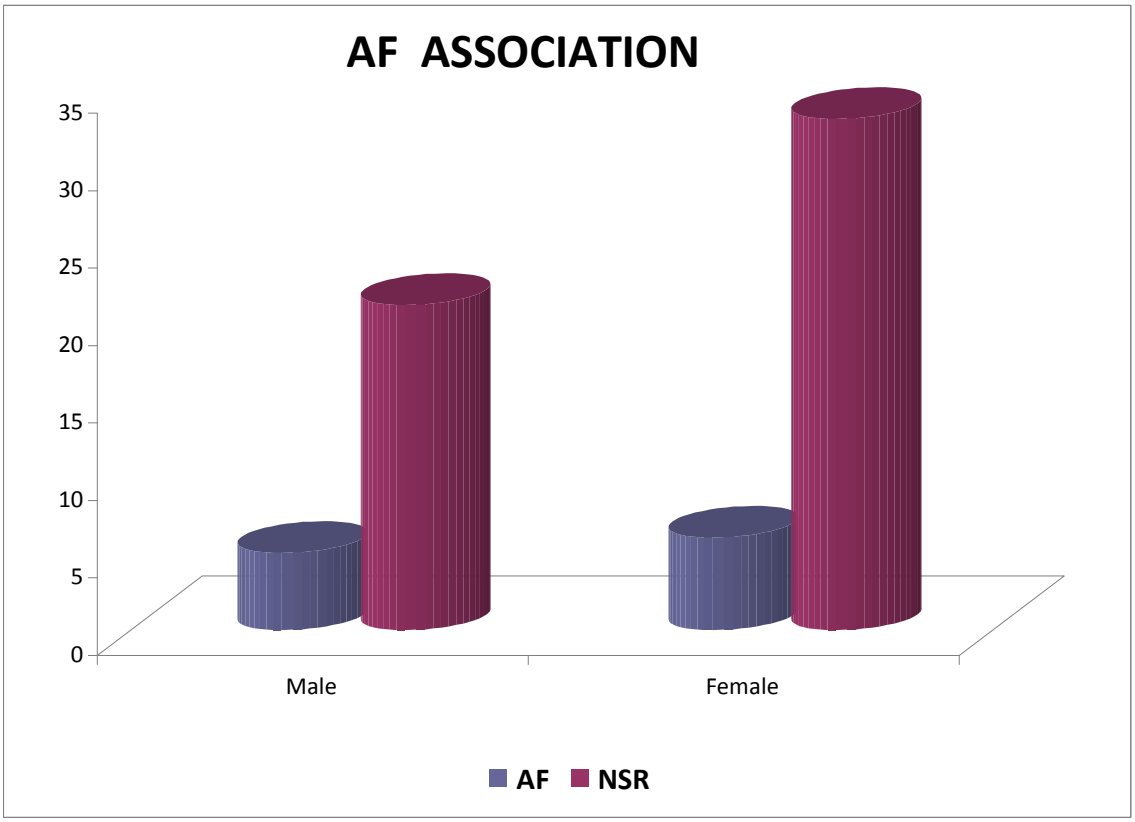

AF ASSOCIATION
35
30
25
20
15
10
5
0
Male
Female
AF
NSR

Table-4

LA Dimension

	Male	**Female**	**Total**	**Significant**
	Mean ± sd	**Mean ± sd**	**Mean ± sd**	(Male Vs Female)
LA Dimension In cm.	4.24 ± 0.89	4.25 ± 0.67	4.24 ± 0.76	t=0.04 df=63 NS

Sd= Standard Deviation NS – Not Significant

The above table shows LA Dimension. Mean LA Dimension between Genders were not differed statistically.

Most of the patients with rheumatic heart disease with mitral valve involvement showed LA size in the mean range of 4.24±0.76.

Also it is found there is no age correlation of AF in RHD patients

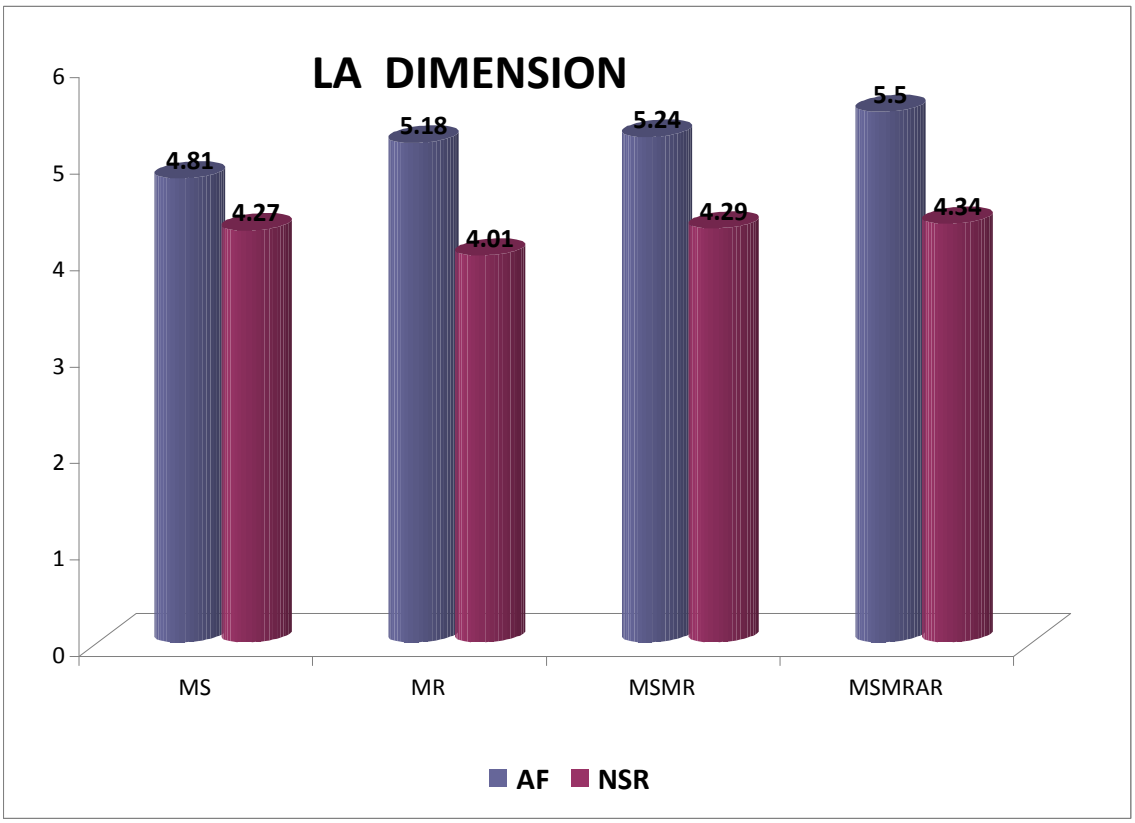

LA DIMENSION
6
5
4
3
2
1
0
4.81
4.27
5.18
4.01
5.24
4.29
5.5
4.34
MS
MR
MSMR
MSMRAR
AF
NSR

Table-5

MS

	Male		**Female**		**Total**	
	N	**%**	**N**	**%**	**N**	**%**
Not Present	11	42.31	6	15.38	17	26.15
Present	**15**	**57.69**	**33**	**84.62**	**39**	**73.85**
	Chi square =5.86 df=1 p <0.02					

Majority of females 33 (84.62%) have MS while comparing males 15 (57.69 %). The distribution between Gender and MS differed statistically (P <0.02).

TABLE-6

MR

	Male		**Female**		**Total**	
	N	**%**	**N**	**%**	**N**	**%**
Not Present	10	38.46	20	51.28	30	46.15
Present	16	61.54	19	48.72	35	53.85
Total	**26**	**100**	**39**	**100**	**65**	**100**
	Chi square =1.03 df=1 NS					

Above table reveals MR status of the Gender. From the above we can say presence of MR is higher in Males 16 (61.54%) then females 19 (48.72%). The difference is statistically not significant.

TABEL-7

AR

	Male		**Female**		**Total**	
	N	**%**	**N**	**%**	**N**	**%**
Not Present	18	69.23	21	53.85	39	60.00
Present	8	30.77	18	46.15	26	40.00
Total	**26**	**100**	**39**	**100**	**65**	**100**
	Chi square =1.54 df=1 NS					

The above table reveals AR is seen in both the gender but more in females. Difference between gender is statistically not significant.

TABLE-8

Pul HT

	Male		**Female**		**Total**	
	N	**%**	**N**	**%**	**N**	**%**
Not Present	14	53.85	12	30.77	26	40.00
Present	12	46.15	27	69.33	39	60.00
Total	**26**	**100**	**39**	**100**	**65**	**100**
	Chi square =3.46 df=1 NS					

From the above table it is observed the females are more prone to develop Pul HT among RHD patients. Difference in PulHT between gender is statistically not significant.

TABLE-9

CORRELATION OF AF AND SR TO LAA VELOCITY, LA DIMENSION AND D-DIMER LEVEL

Variable	**AF N=11**	**NSR N=54**	**t-value**	**Df**	**significant**
Age (in Years)	34.82 ± 6.52	33.72 ± 10.50	0.33[t]	63	NS
LAA Velocity	40.55 ± 2.84	45.50 ± 8.10	1.99 [t]	63	P< 0.05
LA Dimension	4.81 ± 0.99	4.13 ± 0.66	2.58 [t]	63	P< 0.01
D-dimer	0.50 ± 0.47	0.28 ± 0.14	5.06 [t]	63	P< 0.001

NS-Not significant t– T-value

While comparing AF patient and SR patients; LAA velocity is lower in AF group of patients then SR group of patients, the difference is statistically significant ($p<0.05$); LA dimension is higher in AF patients then SR patients, the difference is statistically significant ($p <0.01$).; in D-dimer level in AF patients are having higher than the SR patients, the difference is statistically significant ($p <0.001$)

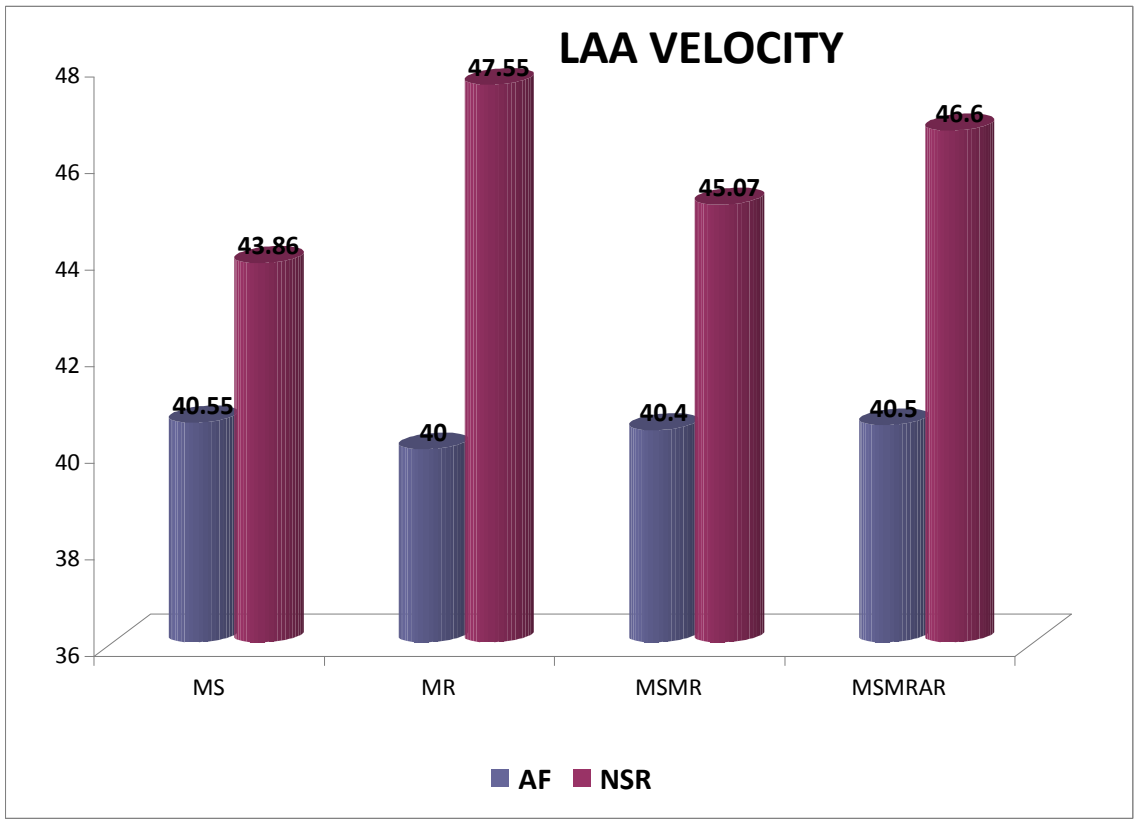

LAA VELOCITY
48
46
44
42
40
38
36
40.55
43.86
40
47.55
40.4
45.07
40.5
46.6
MS
MR
MSMR
MSMRAR
AF
NSR

TABLE-10

CORRELATION OF MS+AF AND MS+SR TO LAA VELOCITY, LA DIMENSION AND D-DIMER LEVEL

Variable	MS+AF N=11	MS+SR N=37	t-value	Df	significant
Age (in Years)	34.82 ± 6.52	35.62 ± 10.87	0.23[t]	46	NS
LAA Velocity	40.55 ± 2.84	43.86 ± 9.08	1.18 [t]	46	NS
LA Dimension	4.81 ± 0.99	4.27 ± 0.67	2.09 [t]	46	P< 0.04
D-dimer	0.50 ± 0.47	0.30 ± 0.15	2.27 [t]	46	P< 0.03

While comparing MS+AF patient and MS+SR patients; LAA velocityy is lower in MS+AF group of patients then MS+SR group of patients, the difference is not statistically significant; LA dimension size is higher in MS+AF patients then MS+SR patients, the difference is statistically significant ($p<0.04$).; in D-dimer score MS+AF patients are having higher level than the MS+SR patients, the difference is statistically significant ($p <0.03$).

TABLE-11

CORRELATION OF MR+AF AND MR+SR TO LAA VELOCITY, LA DIMENSION AND D-DIMER LEVEL

Variable	MR+AF N=6	MR+SR N=29	t-value	Df	significant
Age (in Years)	34.33 ± 6.80	29.03 ± 9.54	0.60[t]	33	NS
LAA Velocity	40.00 ± 1.26	47.55 ± 4.66	0.87 [t]	33	NS
LA Dimension	5.18 ± 0.93	4.01 ± 0.63	1.65 [t]	33	NS
D-dimer	0.52 ± 0.05	0.26 ± 0.13	1.94 [t]	33	NS

The above table reveals MR associated with SR, the D-dimer levels are comparatively lower than when associated with AF.

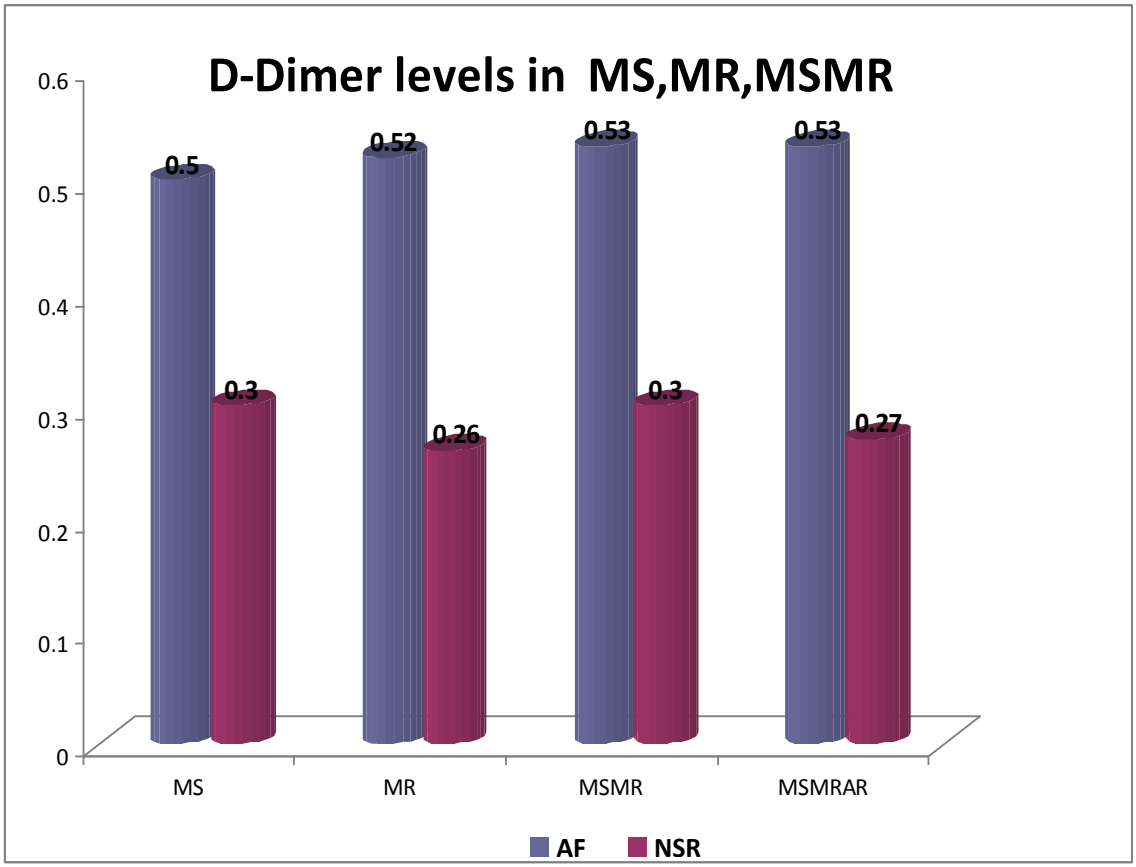

D-Dimer levels in MS,MR,MSMR
0.6
0.5
0.4
0.3
0.2
0.1
0
0.5
0.3
0.52
0.26
0.53
0.3
0.53
0.27
MS
MR
MSMR
MSMRAR
AF
NSR

TABLE-12

CORRELATION OF MS+MR+AF AND MS+MR+SR TO LAA VELOCITY, LA DIMENSION AND D-DIMER LEVEL

Variable	**MSMR+AF N=5**	**MSMR+SR N=15**	**t-value**	**Df**	**significant**
Age (in Years)	35.20 ± 7.23	29.73 ± 10.51	1.07^{t}	18	NS
LAA Velocity	40.40 ± 0.89	45.07 ± 5.20	1.96^{t}	18	P<0.05
LA Dimension	5.24 ± 1.03	4.29 ± 0.97	1.87^{t}	18	NS
D-dimer	0.53 ± 0.04	0.30 ± 0.17	2.95^{t}	18	P<0.01

From the above table shows that LAA Velocity is significantly differ in MSMR+AF than the MSMR+SR patients ($p < 0.05$). D-dimer level is shows statistically significant difference between MSMR+AF and MSMR+SR ($P < 0.01$).

TABLE-13

CORRELATION OF MS+MR+AR+AF AND MS+MR+ AR+SR TO LAA VELOCITY, LA SIZE AND D-DIMER LEVEL

Variable	**MSMRAR+AF N=4**	**MSMRAR+SR N=5**	**t-value**	**Df**	**significant**
Age (in Years)	36.25 ±7.89	34.60 ±13.43	0.22	7	NS
LAA Velocity	40.50 ±1.00	46.60 ±8.02	1.49	7	NS
LA Dimension	5.50±0.98	4.34 ± 0.75	2.02	7	NS
D-dimer	0.53± 0.05	0.27 ± 0.20	2.51	7	P< 0.05

Association of AR to mitral stenosis and regurgitation lesion does not make much difference

DISCUSSION

In this study, an investigation was made into “RHD” patients with various subsets with or without rhythm disturbances with plasma D-dimer levels. And its correlation also done to other variables to LA linear dimension and LAA contraction velocity.

It was analysed that plasma D-dimer levels were significantly higher in patients “RHD” with MS with AF group and significantly lower in “RHD” with MR with SR group .But when associated with MR the results are equivocal.

The results of the present study supported the hypothesis that severe MR decreases coagulation activity and thrombus formation in the left atrium of patients with AF or MS by increasing the shear stress on the left atrial wall, and creating a high-flow wash-out jet which inhibits thrombogenesis on a mechanical basis.

Plasma D-dimer levels provide a sensitive assay for monitoring this process. Plasma D-dimer levels reflect abnormal intra atrial wall, and creating a high-flow wash-out jet which inhibits thrombogenesis on a

mechanical basis. Plasma D-dimer levels provide a sensitive assay for monitoring this process. Plasma D-dimer levels reflect abnormal intra atrial hemodynamics and also the risk of clotting.

Both, AF and MS, cause the stagnation of blood in the left atrium and activate the coagulation system. This in turn cause intra cardiac SEC formation and /or thrombus formation and a decreased blood flow velocity. These hemodynamic events increase the plasma levels of D-dimer, tissue plasminogen activator inhibitor-1 and von Willebrand factor in the peripheral circulation.

Sample implies most of the patients are in middle aged and among them female and male ratio is not statistically significant. Added that sample less than 20 yrs old is only 7%. The Atrial fibrillation was present in 17% of individuals in our study.

In Isolated MS various study showed AF prevalence of 20 to 40%. In Isolated MR prevalence is 15 to 30%. In this study atrial fibrillation found in both sexes is not statistically significant. Chang et.al found that

there was no difference in frequency of AF with reference to sex. Nadeem et.al, showed some difference.

The study also showed that LA dimension is increased in all the samples with mitral valve involvement with a mean value of 4.24 ± 0.76. Normal LA dimension for age adjusted value is 1.8 to 4 cm (3.1 ± 0.5 cm) by Hirata et.al., and Brown et.al., showed 2.3 to 4.4 cm and showed a linear correlations to age and dimension.

When AF present in the sample it is observed there is increased LA size and decreased LAA velocity noted. Correspondingly plasma D-dimer level noted more than 0.45 microgram FEU/ml in these patients which is statistically significant.

Like wise it is observed mitral stenotic patients when associated with AF showed increased LA size and decreased LAA velocity and increased plasma D-dimer level which are statistically significant. In this study highest level are found in the MS+MR+AF subset of patients comparing other groups and lower levels are found in MR+SR group.

STUDY LIMITATIONS

The primary limitation was the small number of patients in each group, which limited the statistical power of the study.

Second, TTE cannot exclude the presence of small thrombi which might affect D-dimer levels; hence, TEE might have been a useful addition for measuring left atrial appendage velocities, the prevalence of the SEC, and thrombus formation.

Third, although D-dimer levels reflect the extent of the thrombotic state very well, other markers (e.g. fibrinogen, PAI-1, / tPA) would have improved the analysis of these patients.

Fourth, a turbidimetric test was used for plasma D-dimer assessments in this study. Although ELISA-based D-dimer assays are considered the ‘gold standard’, others have shown that selected latex turbidimetric assays produce results comparable to those with ELISA and the present results can be considered valid.

Although Rudnicka et.al reported a 10% diurnal variation D-dimer levels in a cohort of 9,377 men and women aged 45 years. In the present study all blood samples were obtained during the early morning. No power calculations were performed.

Finally, although a through history and physical examination was carried out on each study participant to rule out deep venous thromboembolism, the subjects were not screened by Doppler examination. It is difficult, however, even with Doppler, to rule out subclinical venous thromboembolic disease in these patients.

Despite these limitations, the study merits attention, notably as a direct comparison among patient groups with various sub types of mitral valve disease associated with rhythm disturbances and aortic valve involvement.

CONCLUSION

RHD is one among the cause to give more morbidity and mortality in the developing countries.

Presence of Atrial fibrillation worsen the situation as it may lead to more thromboembolic manifestation than age matched controls.

Added the variables in the study like increased LA size and decreased LAA velocity increase the risk of thrombus formation among the subsets of RHD patients.

The presence of moderate to severe MR reduces the risk of thromboembolic manifestation as evidenced by decreased plasma D-imer level in these subsets of these patients indicating systemic hypofibrinolytic state.

In the subset MS+MR+AF association predict a greatest risk among the RHD patients inspite of MR for thromboembolism.

It was concluded that plasma D-dimer level in these patients can predict thromboembolic risk to some extent.

BIBLIOGRAPHY

1. Kario K, Matsuo T, Kobayashi H. Which factors affect high D-dimer levels in the elderly? Thromb Res 1991;62:501-508
2. Kelly J, Rudd A, Lewis RR, Hunt BJ. Plasma Ddimers in the diagnosis of venous thromboembolism Arch Intern Med 2002;162:747-756
3. Sie P. The value of laboratory tests in the diagnosisof venous thromboembolism. Haematologica 1995;80(2 Suppl.):57-60
4. Lip GY, Lowe GD. Fibrin D-dimer: A useful clinical marker of thrombogenesis? Clin Sci (Lond) 282 *Mitral regurgitation and left atrial thrombosis C. Cevik et al.* J Heart Valve Dis Vol. 18. No. 3 May 2009
5. Roldan V, Marin F, Marco P, Martínez JG, Calatayud R, Sogorb F. Hypofibrinolysis in atrial fibrillation. Am Heart J 1998;136:956-960
6. Shrestha NK, Moreno FL, Narciso FV, Torres L, Calleja HB. Two-dimensional echocardiographic diagnosis of left-atrial thrombus in

rheumatic heart disease. A clinicopathologic study. Circulation 1983;67:341-347

7. Aschenberg W, Schluter M, Kremer P, Schröder E, Siglow V, Bleifeld W. Transesophageal two-dimensional echocardiography for the detection of left atrial appendage thrombus. J Am Coll Cardiol 1986;7:163-166
8. Hwang JJ, Chen JJ, Lin SC, et al. Diagnostic accuracy of ransesophageal echocardiography for detecting left atrial thrombi in patients with rheumatic heart disease having undergone mitral valve operations. Am J Cardiol 1993;72:677-681
9. Hwang JJ, Kuan P, Lin SC, et al. Reappraisal by transesophageal echocardiography of the significance of left atrial thrombi in the rediction of systemic arterial embolization in rheumatic mitral
10. valve disease. Am J Cardiol 1992;70:769-773
11. Koca V, Bozat T, Akkaya V, et al. Left atrial thrombus detection with multiplane transesophageal echocardiography: An

echocardiographic study with surgical verification. J Heart Valve Dis 1999;8:63-66

12. Cinar CS, Gurgun C, Nalbantgil S, Can L, Turkoglu C. Relationship between echocardiographic determinants of left atrial spontaneous echo contrast and thrombus formation in patients with rheumatic mitral valve disease. Echocardiography1999;16:331-338
13. Leung DY, Davidson PM, Cranney GB, Walsh WF. Thromboembolic risks of left atrial thrombus detected by transesophageal echocardiogram. Am J Cardiol 1997;79:626-629
14. Tabata T, Oki T, Fukuda N, et al. Influence of aging on left atrial
15. Appendage flow velocity patterns in normal subjects. J Am Soc Echocardiogr 1996;9:274–80.
16. Pollick C, Taylor D. Assessment of left atrial appendage function by transesophageal echocardiography: implications for the development of thrombus. Circulation 1991;84:223–31.

17.16.Fatkin D, Feneley MP. Patterns of Doppler-measured blood flow velocity in the normal and fibrillating human left atrial appendage. Am Heart J 1996;132:995–1003.

18.17. Fatkin D, Kelly RP, Feneley MP. Relations between left atrial appendage blood flow velocity, spontaneous echocardiographic contrast and thromboembolic risk in vivo. J Am Coll Cardiol 1994;23: 961–9.

18. Garcia-Fernandez MA, Torrecilla EG, San Roman D, et al. Left atrial appendage Doppler flow patterns: implications on thrombus formation.Am Heart J 1992;124:955– 61.

19.Jue J, Winslow T, Fazio G, Redberg RF, Foster E, Schiller NB. Pulsed Doppler characterization of left atrial appendage flow. J Am Soc Echocardiogr 1993;6:237– 44.

20.Ito T, Suwa, Hirota Y Influence of left atrial function on Doppler transmitral and pulmonary venous flow patterns in dilated and ypertrophic cardiomyopathy: evaluation of left atrial appendage

function by transesophageal echocardiography. Am Heart J 1996;131:122–30.

21. Ito T, Suwa M, Otake Y, Moriguchi A, Hirota Y, Kawamura K. Left ventricular Doppler filling pattern in dilated cardiomyopathy: relation to hemodynamics and left atrial function. J Am Soc Echocardiogr 1997;10:518 –25.

22. Chan SK, Kannam JP, Douglas PS, Manning WJ. Multiplane transesophageal echocardiographic assessment of left atrial appendage anatomy and function. Am J Cardiol 1995;76:528 –30.

23. Mu¨gge A, Kuhn H, Nikutta P, Grote J, Lopez JA, Daniel WG. Assessment of left atrial appendage function by biplane transesophageal

24. Echocardiography in patients with nonrheumatic atrial fibrillation: dentification of a subgroup of patients at increased embolic risk. J Am Coll Cardiol 1994;23:599 – 607.

25. 24. Appleton CP, Jensen JL, Hatle LK, Oh JK. Doppler evaluation of left and right ventricular diastolic function: a technical guide for

obtaining optimal flow velocity recordings. J Am Soc Echocardiogr 1997;10: 271–92. Carranza C, Abufhele A, Cartes F, Forero A. Transthoracic versus transesophageal two-dimensional echo Doppler evaluation of flow velocity in the left atrial appendage. Echocardiography 1997;14:357– 61.

26. Wanishsawad C, Weathers LB, Puavilai W. Mitral regurgitation and left atrial thrombus in rheumatic mitral valve disease. A clinicopathologic study. Chest 1995;108:677-681

27. Movsowitz C, Movsowitz HD, Jacobs LE, Meyerowitz CB, Podolsky LA, Kotler MN. Significant mitral regurgitation is protective against left atrial spontaneous echo contrast and thrombus as assessed by transesophageal echocardiography. J Am Soc Echocardiogr 1993;6:107-114

28. Blackshear JL, Pearce LA, Asinger RW, et al. Mitral regurgitation associated with reduced thromboembolic events in high-risk patients with nonrheumatic atrial fibrillation. Stroke Prevention in Atrial Fibrillation Investigators. Am J Cardiol 1993;72: 840-843

29. Hwang JJ, Shyu KG, Hsu KL, Chen JJ, Kuan P, Lien WP. Significant mitral regurgitation is protective against left atrial spontaneous echo contrast formation, but not against systemic embolism. Chest 1994;106:8-12

30. Karatasakis GT, Gotsis AC, Cokkinos DV. Influence of mitral regurgitation on left atrial thrombus and spontaneous echocardiographic contrast in patients with rheumatic mitral valve disease. Am J Cardiol 1995;76:279-281

31. Ozkan M, Kaymaz C, Kirma C, et al. Predictors of left atrial thrombus and spontaneous echo contrast in rheumatic valve disease before and after mitral valve replacement. Am J Cardiol 1998;82:1066-1070

32. Kaymaz C, Ozdemir N, Cevik C, et al. Effect of paravalvular mitral regurgitation on left atrial thrombus formation in patients with mechanical mitral valves. Am J Cardiol 2003;92:102-105

33. Lip GY, Lowe GD, Rumley A, Dunn FG. Increased markers

of thrombogenesis in chronic atrial fibrillation: Effects of warfarin treatment. Br Heart J 1995;73:527-533

34. Yamamoto K, Ikeda U, Seino Y, et al. Coagulation activity is increased in the left atrium of patients with mitral stenosis. J Am Coll Cardiol 1995;25: 107-112

PROFORMA

Serial No: Date:

Name: Age: Sex: Wt

Address:

Diagnosis:

ECG: NSR/AF

Any Medication:

Co Morbidity

Personal H/O Smoker Alcoholic

ECHO LA Dimension Echo Auto Contest

LA Clot LAAVelocity

MS Severity MVO Mild Mod Severe

MR Severity Mild Mod Severe

AS AR

LVEF% Pul HT TR Velocity

D-dimer Level

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Assessment of Prothrombolic Burden in Patients with Rheumtic mitral valve Disease using Plasma of d-dimer Assay

Principal Investigator : Dr.P.Sampath Kumr

Designation : PG in DM(Cardio)

Department : Department of Cardiology
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 06.03.2012 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate form the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

08/03/12

MEMBER SECRETARY,
IEC, SMC, CHENNAI

MASTER CHART

IDNO	Name	Age	SEX	WEIGHT	HEIGHT	ECG	LA DIMENSION cm	LAA VELOCITY cm/sec	MVO	MS	MR	AS	AR	LV	PUL_HT	D_DIMER µgm/ml-FEU
1	RAJASEKARAN	21	M	52	160	NSR	3.80	53.00	2.80	NIL	Severe	NIL	NIL	N	Mild	0.31
2	DHINESH GOWSIK	15	M	48	156	NSR	4.60	51.00	1.80	Mild	Severe	NIL	Severe	N	Mild	0.09
3	GEETHA	27	F	50	158	NSR	3.50	45.00	3.10	NIL	Mild	NIL	Mild	N	Mild	0.30
4	PUSHPA	40	F	59	151	AF	5.70	42.00	0.90	Severe	Mild	Mild	Mild	N	Mild	0.48
5	ARUNACHALAM	46	M	58	165	AF	6.00	40.00	1.10	Mod	NIL	NIL	NIL	N	Mod	0.50
6	BHASKER	26	M	68	158	NSR	4.30	42.00	3.10	NIL	Mild	NIL	NIL	N	NIL	0.54
7	GOWRI	50	F	62	163	NSR	4.30	50.00	1.80	Mild	NIL	NIL	Mod	N	Mild	0.13
8	GOMALA	45	F	39	140	NSR	5.60	42.00	0.70	Severe	NIL	Severe	Mod	N	Mild	0.34
9	ANJAMMAL	44	F	55	154	NSR	4.50	54.00	1.30	Mod	NIL	Severe	Mod	N	Mild	0.32
10	MAHESH	27	M	60	158	NSR	4.80	50.00	1.80	Mild	NIL	NIL	NIL	N	NIL	0.20
11	MUTHULAKSHMI	27	F	41	144	NSR	5.10	38.00	1.10	Mod	Mild	NIL	Mild	N	Mild	0.32
12	KANNAGI	19	F	48	154	NSR	3.60	48.00	1.90	Mild	Mild	NIL	NIL	N	NIL	0.12
13	MARIAMMAL	45	F	66	154	NSR	4.40	38.00	1.30	Mod	NIL	NIL	Mod	N	Mild	0.52
14	PRABHAGAR	31	M	60	162	NSR	4.40	50.00	2.80	NIL	Mild	NIL	NIL	N	NIL	0.24
15	BALA	26	F	40	144	NSR	4.80	48.00	0.90	Severe	Mild	NIL	NIL	N	Mild	0.09
16	MURALI	19	M	52	161	NSR	3.80	48.00	1.90	Mild	Mild	NIL	NIL	N	NIL	0.29
17	THIRUVENGADAM	45	M	45	167	AF	6.80	40.00	1.30	Mod	Severe	NIL	Mild	N	Severe	0.52
18	PARIMALA	23	F	54	156	NSR	4.30	52.00	1.70	Mild	Mod	NIL	NIL	N	Mild	0.42
19	LATHA	40	F	52	157	NSR	4.80	38.00	1.40	Mod	Mild	Mod	Mod	N	Mod	0.58
20	salini	32	F	55	154	AF	4.00	42.00	1.30	Mod	NIL	NIL	NIL	N	Mild	0.52
21	SHOBA	18	F	50	149	NSR	3.20	55.00	3.10	NIL	Mod	NIL	NIL	N	NIL	0.41
22	PRAKASH	30	M	60	155	NSR	4.20	52.00	3.10	NIL	Mild	NIL	NIL	N	NIL	0.13
23	RAMANI	26	F	60	158	NSR	3.80	40.00	1.40	Mod	NIL	NIL	NIL	N	NIL	0.25
24	THILAGAM	49	F	58	164	NSR	3.30	46.00	1.80	Mild	NIL	Mild	Mod	N	Mild	0.32
25	VIJAYALAKSHMI	36	F	49	161	NSR	4.50	45.00	1.00	Severe	NIL	Mod	Mild	N	Severe	0.38
26	LOKESH	27	M	51	158	NSR	4.00	42.00	1.70	Mild	NIL	NIL	NIL	N	Mild	0.42
27	NASREEN	28	F	49	152	NSR	5.10	40.00	2.10	Mild	Mod	NIL	NIL	N	NIL	0.19
28	RAJAN	39	M	51	158	NSR	3.60	44.00	1.80	Mild	Mild	NIL	NIL	N	Mild	0.32

29	SARAVANAN	33	M	48	161	AF	4.90	40.00	1.00	Severe	Mod	NIL	Mod	N	Mod	0.60
30	VIDYA	29	F	55	160	NSR	4.20	48.00	2.80	NIL	Mod	NIL	NIL	N	NIL	0.14
31	VIGNESWARI	54	F	60	156	NSR	4.20	51.00	1.80	Mild	NIL	NIL	NIL	N	NIL	0.21
32	RAJU	38	F	48	158	NSR	3.80	36.00	0.90	Severe	NIL	NIL	NIL	N	Mod	0.48
33	SELVI	48	F	52	140	NSR	3.20	51.00	1.80	Mild	Mild	NIL	Mild	N	Mod	0.23
34	SOMU	42	M	61	159	NSR	3.90	50.00	2.90	NIL	Mild	NIL	NIL	N	NIL	0.26
35	SIVAN	30	M	50	163	NSR	3.60	52.00	3.20	NIL	NIL	NIL	Mild	N	NIL	0.14
36	JERINA	22	F	38	148	NSR	3.20	49.00	1.90	Mild	Mild	NIL	NIL	N	NIL	0.18
37	VALLI	26	F	60	152	NSR	3.80	46.00	2.80	NIL	Mild	NIL	NIL	N	NIL	0.31
38	CHELLAMAL	45	F	55	155	NSR	5.10	45.00	3.10	NIL	Severe	NIL	NIL	N	NIL	0.13
39	PANDURENGAN	30	M	60	161	AF	4.90	38.00	1.20	Mod	Mild	NIL	NIL	N	Mild	0.45
40	LALITHA	27	F	55	159	AF	4.60	40.00	0.90	Severe	Mild	NIL	Mild	N	Mod	0.52
41	SUNDARI	42	F	54	148	NSR	3.80	54.00	1.90	Mild	NIL	NIL	NIL	N	NIL	0.21
42	KUMAR	43	M	66	159	NSR	4.00	55.00	1.45	Mod	Mild	NIL	Mild	N	Mild	0.13
43	GOMATHI	28	F	48	157	AF	4.30	38.00	1.40	Mod	NIL	NIL	Mild	N	Mod	0.42
44	REVENAIAH	42	M	51	162	NSR	4.00	40.00	1.30	Mod	Mild	NIL	NIL	N	Mod	0.45
45	PURUSHOTH	33	M	67	162	NSR	3.80	34.00	1.10	Mod	NIL	NIL	NIL	N	NIL	0.03
46	KALAI	23	F	49	153	NSR	4.20	38.00	0.90	Severe	NIL	NIL	NIL	N	Mod	0.52
47	JAIGANESH	40	M	65	162	NSR	3.20	50.00	3.10	NIL	NIL	NIL	Mild	N	NIL	0.13
48	KAMESH	26	M	64	160	NSR	3.20	46.00	2.80	NIL	Mod	NIL	Mild	N	NIL	0.23
49	RAMU	38	F	45	161	AF	3.70	48.00	0.80	Severe	NIL	NIL	NIL	N	Mod	0.48
50	SHANKER	14	M	43	150	NSR	3.10	52.00	3.20	NIL	Mild	NIL	NIL	N	NIL	0.32
51	VALARMATHI	31	F	44	152	AF	4.20	40.00	1.20	Mod	Mild	NIL	NIL	N	Mod	0.53
52	ARUNACHALAM	46	M	58	165	NSR	6.00	4.00	1.10	Mod	NIL	NIL	NIL	N	Mod	0.30
53	SOMU	42	M	61	159	NSR	3.90	50.00	2.90	NIL	Mild	NIL	NIL	N	NIL	0.26
54	PURUSHOTH	33	M	67	162	AF	3.80	38.00	1.10	Mod	NIL	NIL	NIL	N	NIL	0.50
55	LOKESH	27	M	51	158	NSR	4.00	42.00	1.70	Mild	NIL	NIL	NIL	N	Mild	0.42
56	RAJESHWARI	50	F	62	163	NSR	4.30	50.00	1.80	Mild	NIL	NIL	Mod	N	Mild	0.13
57	ANURADHA	44	F	55	154	NSR	4.50	54.00	1.30	Mod	NIL	Severe	Mod	N	Mild	0.32
58	BALACHANDRAN	26	F	40	144	NSR	4.80	48.00	0.90	Severe	Mild	NIL	NIL	N	Mild	0.09
59	MUNIAMMA	45	F	66	154	NSR	4.40	38.00	1.30	Mod	NIL	NIL	Mod	N	Mild	0.52
50	KAMALA	45	F	39	140	NSR	5.60	42.00	0.70	Severe	NIL	Severe	Mod	N	Mild	0.34
61	RANJU	38	F	48	158	NSR	3.80	36.00	0.90	Severe	NIL	NIL	NIL	N	Mod	0.48
62	SIVARAJAN	30	M	50	163	NSR	3.60	52.00	3.20	NIL	NIL	NIL	Mild	N	NIL	0.14

63	JASMINE	22	F	38	148	NSR	3.20	49.00	1.90	Mild	Mild	NIL	NIL	N	NIL	0.18
64	MALLIGA	26	F	60	152	NSR	3.80	46.00	2.80	NIL	Mild	NIL	NIL	N	NIL	0.31
65	DHANALAKSHMI	45	F	66	154	NSR	4.40	38.00	1.30	Mod	NIL	NIL	Mod	N	Mild	0.52

ABSTRACT

Assessment of Prothrombotic Burden in the Rheumatic heart disease with various subset

Background : RHD is more common in middle aged in dividuals with stroke manifestation . Among the subset of patients with RHD it is more commonly associated in MS with AF patients. And it is more common when increased LA Size as well as decreaesd LAA empting Velocity. So our study evaluated the correlation

Method. Blood sample collected to this patients with RHD with excluding older age, H/o surgery and DVTand Recent trauma. D-dimer assayed by particle enhanced immunoturbidimetry. Echo done to all patients.

Results: It was analysed that age distribution is in the range of 33.91to 9.91.With AF Association present in 16.92% of the Individual. Mean LA dimension in all subsets in the range of 4.47± 0.82. D-dimer level is highest in the subset of MS + MR + AF subgroup 0.53± 0.04 µgm FEU/ ml.

Conclusion: It was concluded the highest D-dimer level found in MS+MR+AF group and lower in MS+SR group. Presensce of MR dose not prevent thromboembolism when associated With AF and MS.