EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 9
300-305
Year: 2016

EFFECTS OF REPEATED PREGNANCIES ON LEFT VENTRICULAR MUSCLE MASS IN INDIAN POPULATION

[*1]Dr. Satyam Chakraborty, [2]Anirban Sinha, [3]Dr. Lakshmi Dey, [4]Dr. Praveen Devarbhavi and [5]Kingshuk Bhattacharjee

[1,3,4]DM Post-Doctoral Trainee, Department of Endocrinology and Metabolism, Medical College and Hospital, 88, College Street; Kolkata-700073.
[2]Assistant Professor, Department of Endocrinology and Metabolism, Medical College and Hospital, 88, College Street; Kolkata-700073.
[5]Assistant Manager, Medical Services, Biocon Limited, Tower-3, Semicon Park, Electronic city, Phase 2, Bangalore.

*** Corresponding Author: Dr. Satyam Chakraborty**
DM Post-Doctoral Trainee, Department of Endocrinology and Metabolism, Medical College and Hospital, 88, College Street; Kolkata-700073.

Article Received on 22/06/2016 **Article Revised on 13/07/2016** **Article Accepted on 02/08/2016**

ABSTRACT

Background: Nothing much is known on the cardiological alterations that pregnancy bestows on an Indian female and whether these cardiological alterations reverse completely after the pregnancy episode is over and more so if these alterations leave any residual sequel in repeated episodes which may cause increased cardiological morbidity in Indian females. **Aims:** To assess the echo-cardiographic alterations in left ventricle due to repeated pregnancies in Indian population. **Materials and Methods: A c**ross-sectional observational study with 150 Antepartum & Post-partum female patients coming for outdoor visits was randomly selected between September 2010 & October 2011. Respiratory & cardiological parameters were studied clinically by respiratory rate measurements at rest and after 6 –minute walk test. Electro-cardiographic assessments were done to rule out ST – Depression, T-Wave Inversions or any P-Wave abnormalities taking into account the changes in Axis which pregnancy itself can cause. Echo-cardiographic alterations in left ventricle were studied as per the study objective. **Results:** Number of Subjects having gravida smaller than 3 is 93 whereas the number of Subjects having gravida greater than or equal to 3 is 57. Subjects having gravida of not more than 2 having significant LV Mass is minimal but the situation changes drastically after gravida of 3 & above. After Gravida 5 the % of significant LV Mass (Ante-partum & Post-partum) is 100%,although the data strength is only of 10 Subjects. Based on the data given after 45 days of post pregnancy, it can be claimed with 95.5% confidence level that the LV mass would be within the following range for the specified gravida level. Thus from the present study, we state that with 95% confidence level we can say that if a patient's gravida level is 1, her LV mass would be in the range of 82.44 --- 153.16 gm. Similarly, If the gravida level is 2 LV mass would be within 79.4 – 190.13 and if the gravida level is 3 LV mass would be within 109.62 – 192.02. If the gravida level is 4 LV mass would be within 97.52 – 214.76, If the gravida level is 5 LV mass would be within 131.99 – 277.50 , If the gravida level is 6 LV mass would be within 149.24 – 269.89 , If the gravida level is 7 LV mass would be within 167.36 – 236.78. **Conclusion:** Since the risk associated to LV mass appears to be progressive, without a clear threshold, additional input can be added at different baseline risks, defined by the prevalence of other known cardiovascular risk factors. The addition of multiple newer markers, however, leads to a small increment in risk stratification capacity over formulas applying only classical risk factors. Despite these limitations, the role of echocardiography in LV mass determination is of great clinical value. Considering all the aspects, use of echocardiography in clinical studies must be standardized applying already defined criteria. In delineating a study, if two-dimensional is impractical, then two-dimensional guided M-mode, using ASE criteria and Devereux modified formula, may allow estimation of LV mass with an acceptable level of accuracy.

KEYWORDS: LV Mass, Gravida, Pregnancy, Echocardiography.

INTRODUCTION

The physiological process of pregnancy causes significant alterations in the haemodynamic profile. A lot of literatures have stated the various aspects of the changes.[1] However; only a few studies have talked about any cardiological alterations and more so none of them have been performed in the Indian sub-continent.[2] Indian women differ a lot anatomically, physiologically as well as socio-culturally from their Western counterparts. Average Body weight of Indian Female is

50kg whereas that in U.S.A is around 70-73 kgs. Average Height of Indian female is 152cms whereas that of her U.S counterpart is 163 cms. Even the hemoglobin levels vary being around 13-15gm/dl in westerners & 10-11 gm/dl in Indian females. A lot of other parameters also suggest the more tensile stature of westerners to overcome the physiological stress of pregnancy unlike their Indian counterpart. The basic problems of Poverty, malnutrition, under-nutrition, sexual discrimination, nutritional anemia, child-hood marriages followed by childhood pregnancies & finally multiple pregnancies stings the "poor 2 Indian Woman" right from birth. It is therefore not a blind venture if we speculate that an Indian mother will less likely tolerate the physiological stress of pregnancy equally as her western counterpart.[3,4]

In our study we try to concentrate on the cardiological alterations that pregnancy bestows on an Indian Female and if these cardiological alterations reverse completely after the pregnancy episode is over and more so if these alterations leave any residual sequel in repeated episodes which may cause increased Cardiological morbidity in Indian females.

Aims and Objectives

To assess the echo-cardiographic alterations in left ventricle due to repeated pregnancies in Indian population.

Methodology: A cross-sectional study done in Gangori Hospital & SMS Hospital, Jaipur. The cases were those coming for Ante-natal & Post-Natal check-ups in the Hospitals.

- Study type: Observational
- Study Design: Random prospective
- SUBJECTS: 150 Antepartum & Post-partum Female patients coming for outdoor visits were randomly selected between September 2010 & October 2011.
- Examination included medical interview, Vitals, History of presenting illness, Systemic examination, Collection of blood sample, Collection of Urine samples, ECG and 2D-echo

INCLUSION Criteria: - Pregnant women between the age of 20 & 40 years, Normotensive & Nonalbuminuric.
EXCLUSION Criteria: - Pre-existing cardiac disease, Hypertension, Normal thyroid profile, Anaemia (Hb <9 gm %), Chronic kidney disease, COPD, Obesity (BMI>= 27) and Smoker & Alcoholic

A total of 150 patients were selected After Clinical Evaluation to rule out Valvular Heart Disease, Angina or Ischemic Heart Disease, Any chronic lung conditions like Bronchial Asthma, Chronic Airway Obstructive Disease which may significantly alter Cardio-Vascular Haemo-dynamics, Routine Blood investigations & Urine Analysis. Diabetes & Thyroid Abnormalities were screened. Special precautions have been taken to rule out Pregnancy Induced Hypertension(PIH) as they could easily confound the results of the study. PIH has far reaching influence on Cardio-Vascular & Haemo-dynamic profiles during pregnancy. Urine examination for proteinurea, Brachial Blood-Pressure measurements were performed to rule out PIH.

Respiratory & Cadiological Parametres were studied clinically by Respiratory Rate measurements at rest and after 6 –minute walk test. Electro-Cardiographic Assessments were done to rule out ST – Depression, T-Wave Inversions or any P-Wave abnormalities taking into account the changes in Axis which pregnancy itself can cause.

Precautions were taken to screen out patients with Moderate to Severe Anemia as it may interfere with results. According to the consensus of the Joint Committee for plan approval the hemoglobin levels were relaxed to 9gm%. This was done in view of Physiological anemia of Pregnancy & the poor socio-economic status in which Pregnant women thrive in India.

RESULTS

The population size is 150 patients in the present study. Number of Subjects having gravida smaller than 3 is 93 whereas the number of Subjects having gravida greater than or equal to 3 is 57.

Table 1: Characteristics of Study Population

During pregnancy period			PP After 45 days	
Gravida	**No of Subjects**	**No. of Subjects detected to have lv mass >=150gm**	**No of Subjects**	**No. of Subjects detected to have lv mass >=150gm**
1	34	2	11	Nil
2	40	11	8	1
3	13	5	4	4
4	16	10	4	4

Table 2: Relationship between Gravida and LV Mass

Gravida	No of Subjects (1)	No. of Subjects Having LV mass >=150gm (2)	% of Subjects Having LV mass >=150gm (2)/(1)x100%
1	45	2	4.44
2	48	12	25
3	17	9	52.94
4	20	14	70

It is quite evident from the above 2 tabloid illustration the Subjects having Gravida of not more than 2 having significant LV Mass is minimal but the situation changes drastically after Gravida of 3 & above. After Gravida 5 the % of significant LV Mass(Ante-partum & Post-partum) is 100%,although the data strength is only of 10 Subjects.

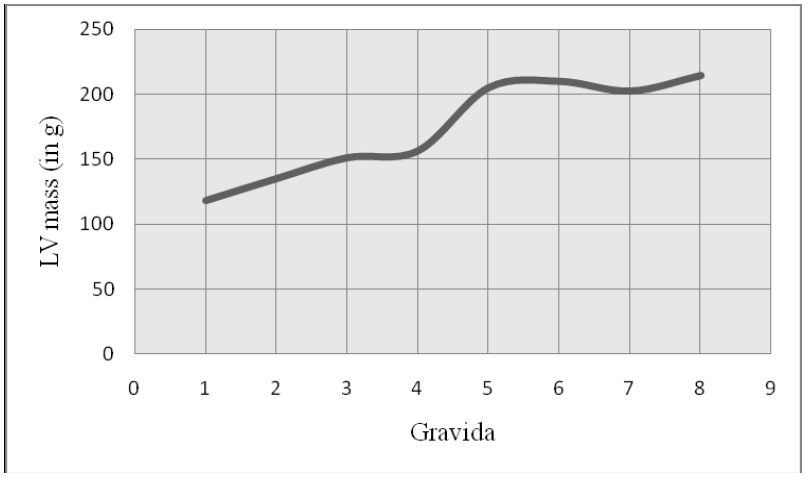

Figure 1: LV Mass/Gravida relationship graph

In figure 1, the LV Mass/Gravida relationship graph shows constant uprising slope with LV Mass crossing 150gms significance limit in & after Gravida of 3 & more. Gravida of 5 & more have average LV Mass well above 190 gms & more.

In our study, percentage of Subjects having a LV Mass >= 150 gms/Gravida depicts an almost 100% Subjects of Gravida >= 5 have crossed the significant LV Mass limits of 150 gms. (Figure 2).

The following Bar-Graph clearly depicts that that there is a significant increase in LV Mass as the pregnancy progresses, more importantly the increased LV Mass do not come down to Base levels (i.e the average LV Mass at 2months of gestation) even after 45 days of Delivery.

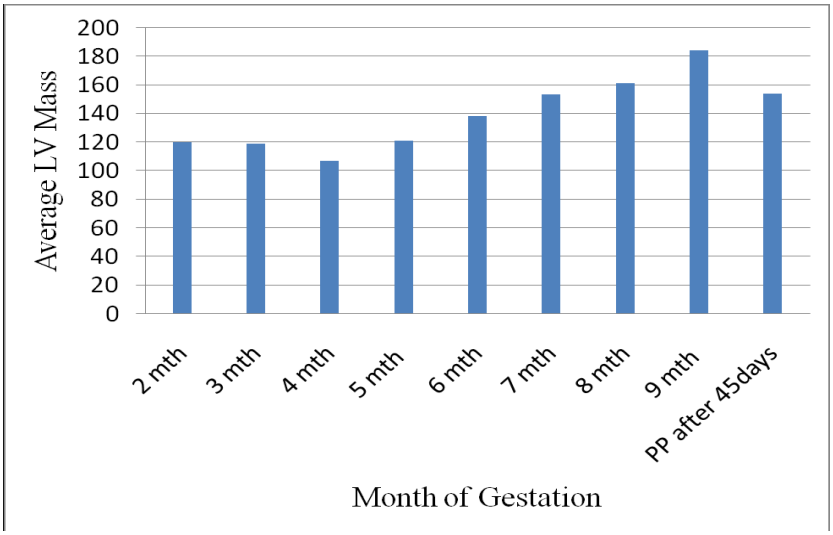

Figure 2: Significant increase in LV Mass as the pregnancy progresses

Based on the data given after 45 days of post pregnanc, it can be claimed with **95.5%** confidence level that the LV mass would be within the following range for the specified gravida level. Thus from the present study, we state that with **95%** confidence level we can say that if a patient's gravida level is 1, her Lv mass would be in the range of 82.44 --- 153.16 gm. Similarly, If the gravida level is 2 LV mass would be within 79.4 – 190.13 and if the gravida level is 3 LV mass would be within 109.62 – 192.02. If the gravida level is 4 LV mass would be within 97.52 – 214.76, If the gravida level is 5 LV mass would be within 131.99 – 277.50 , If the gravida level is 6 LV mass would be within 149.24 – 269.89, If the gravida level is 7 LV mass would be within 167.36 – 236.78.

Table 3: Comparison of During Pregnancy and Post Pregnancy LV Mass Distribution Startified by Gravida

During pregnancy period			PP After 45 days	
Gravida	**No of patients**	**No. of patients detected to have lv mass >=150gm**	**No of patients**	**No. of patients detected to have lv mass >=150gm**
1	34	2	11	Nil
2	40	11	8	1
3	13	5	4	4
4	16	10	4	4
5	8	8	5	5

DISCUSSION

The study entitled Effects of Repeated Pregnancy on Left Ventricular Muscle Mass was conducted in SMS Medical College, Jaipur, Rajasthan. The prime objective behind the study was to evaluate the effects of repeated physiological stress of pregnancy on Left Ventricular Muscle mass & thus obtain a cause & effect relationship between number of pregnancies & Ischemic Heart disease in Indian Female population. The study subjects were 150 female patients who were either pregnant or post-partum who visited ante-natal & post-natal clinics of Gangouri hospital & SMS Hospital. The patients who met the inclusion criteria namely normotensive & non-albuminuric & non-obese within the age-range of 20 & 40 were subjected to routine blood investigations to rule out the confounding variables. The overall prevalence of Coronary Heart Disease in Indian Female population is on the rise. According to the study conducted by Gupta Et.al.[5] In 1977-78, it was around 0.23%, Chadha et. al conducted two repeat surveys in Delhi and documented the incidence of CHD, during 3 year period after initial survey carried out during 1987-90, 2.1% among women remarkably higher than their male counterpart which was 1.73%.[6] Accordingly the all-cause mortality rate, Reddy et.al speculated the rise in mortality of Indian females to rise from 126/100,000 in 1985 to 239/100000 in 2015.[7] Sonjai et.al, in 8th Global Conference of Actuaries suggested that the incidence of CHD was higher in Females than males in India. it is being noticed that the Female projected CHD percentage in Rural India where effective family-planning initiatives are still to penetrate , is reasonably high & quite higher than their male counter-parts. Linda Rosenfeld pointed out that , between the ages of 45 and 64, one in nine women has some form of cardiovascular disease.“ One in three women 96 above the age of 65 has some form of cardiovascular disease. Of the approximately 500,000 fatal heart attacks per year, almost half occur in women.“ Women who have a heart attack are twice as likely to die within the first two weeks as are men. l Within the first year after a heart attack, 39 of women die compared with 31%percent of men. Extensive works have been performed in the literature about the possible risk factors of CHD in Females.

Among the uncontrollable risk factors are i) Family history of premature coronary artery disease or stroke (occurring in male family members younger than 55, or in female family members younger than 65), ii) Age 55 or older, iii) Post-menopausal, or after ovariotomy iv) Pre-eclampsia (significant high blood pressure) or gestational diabetes, low-birth-weight baby & a family history of premature cardiac disease, The controllable risk factors described till date are being overweight or obese, Sedentary lifestyle (little to no exercise), smoking or using tobacco products puts you at risk for a multitude of health problems, including heart disease, high blood pressure, high total cholesterol, and/or low HDL cholesterol, A diagnosis of diabetes, a diagnosis of metabolic syndrome, increased C-reactive protein (CRP) levels, using birth control pills, especially if you are also a smoker.

Left Ventricular Hypertrophy as a strong Risk Factor of CHD

Left Ventricular Hypertrophy has been considered as an individual risk-factor for Coronary Heart Disease in numerous literatures. Brown W et.al in December 2000 investigated 7924 patients aged between 25 & 74 years old, derived from NHANES II mortality trial (1976 – 1992) with Cox Regression analysis. During 16.8 follow-up years, there were 462 (26%) deaths from CHD (ICD-9 410-414) and 667 (38%) deaths from diseases of the heart (ICD-9 390-398, 402, 404, 410-414, 415-417, 420-429). LVH prevalence was 13.3 per 1000 population. Hypertension prevalence was 29.1%. LVH prevalence

was higher among hypertensive adults than among normotensive adults (29.9 vs 6.4 per 1000, P <.001). Persons with LVH were twice as likely to die of CHD (relative risk, 2.0; 95% confidence interval, 1.2, 3.5) and diseases of the heart (relative risk, 1.9; 95% confidence interval, 1.1, 3.0) after adjustment for hypertension and covariates. In age-adjusted predicted survival, probability plots for CHD, and diseases of the heart, normotensives with LVH had survival similar to hypertensive adults with LVH and lower survival than normotensive and hypertensive adults with no LVH.

Similarly Jalal et.al in 1992 examined the association between echo-cardio graphically proved LVH and its relation with Mortality in General & CHD in particular in 785 patients by a Cohort study with a mean follow-up of 99 years. They concluded LVH to be an individual risk-factor for CHD & Mortality.

Left Ventricular Hypertrophy has also been implicated to cause increased Cardio-Vascular deaths from reasons other than CHD. Jalal et.al investigated for Occurrence of Ventricular Arrhythmias in patients of Left Ventricular Hypertrophy without CHD. The frequency and complexity of ventricular arrhythmias were significantly related to the presence of left ventricular hypertrophy whether it was defined by wall thickness (interventricular septum or posterior wall >=1.2 cm) or by left ventricular mass indexed to height (left ventricular mass/height >=163 g/m in men and >=121 g/m in women). The relation between left ventricular mass or wall thickness to ventricular arrhythmia was graded and continuous; for every 1 mm increase in the thickness of interventricular septum or posterior wall there was an associated two to threefold increase, respectively, in the occurrence and complexity of ventricular arrhythmias. In conclusion, left ventricular hypertrophy is associated with an increase in the frequency and complexity of ventricular arrhythmias in the absence of coronary artery disease, and the relation is graded and continuous.

Richard Cooper et.al in 1995 evaluated 436 consecutive black patients (163 men and 273 women) free of angiographic coronary artery disease from a hospital registry. LVH (left ventricular [LV] mass/body surface area ≥117 g/m2 in men and ≥104 g/m2 in women) was present in 84 men (52%) and 119 women (44%). During a mean of 5 years' follow-up (range, 0 to 9), 49 patients (26 men and 23 women) died. The mortality rate was 5.40 per 100 patient-years in men with LVH and 2.58 in men without LVH (crude relative risk [RR]=2.09) and 3.21 and 0.66, respectively, in women (RR=4.87). In Cox regression analysis, adjusting for age, hypertension, and ejection fraction, the RR of total death for LVH versus non-LVH was 2.0 (95% confidence interval [CI], 0.8 to 5.0) in men and 4.3 (95% CI, 1.6 to 11.7) in women. For cardiac death, RR was 1.3 (95% CI, 0.4 to 3.7) and 7.5 (95% CI, 1.6 to 33.8) in men and women, respectively. Analyses using LV mass indexed by height or height with the use of different LVH cut points, comparing patients in the highest sex-specific tertile of mass index to those in the lower two tertiles, and the use of LV mass indexes as continuous variables similarly demonstrated a greater increase in risk of either fatal end point among women than men. The aforementioned study concluded that the risk of fatalities Due to after-effects of LVH is much larger in females in comparison to males. Weber KT et.al also postulated that chronically increased After-load states like hypertension , Aortic Stenosis as well as preload states like chronic anaemia ,Thyrotoxicosis predispose the Heart to Ventricular Hypertrophy, & precipitates Heart Failure. The intricate mechanism involved is the gradual development of myocardial fibrosis which eventually reduce cardiac output. Bots et.al in 2002 investigated the association between electrocardiographically assessed left ventricular hypertrophy (LVH) and fatal, non-fatal, haemorrhagic and ischaemic stroke in four European cohorts participating in EUROSTROKE. They found that LVH was associated with a twofold increased risk of stroke (odds ratio 2.1 (95% CI 1.3 to3.5). The risk was particularly pronounced for fatal stroke (4.0 (95% CI 2.1 to 7.9)), whereas the risk was non-significantly increased for non-fatal stroke (1.5 (95% CI 0.8 to 2.7)) was non-significantly increased for non-fatal stroke (1.5 (95% CI 0.8 to 2.7)). All the above literatures provided depict definite risk of Coronary Heart Disease & subsequent significant morbidity & mortality due to Left Ventricular Hypertrophy. The mortality causes may either be in the face of massive Myocardial Infarction after long-standing Coronary Artery disease or Sudden Cardiac arrest after Ventricular Tachy-arrhythmias or Fatal Cerebro-vascular accidents, or it might be more insidious Heart Failure. Our study has proved Left ventricular Hypertrophy as a direct effect of repeated physiological stress of pregnancy & thus predisposes the large Indian female child-bearing population to future risk of significant Cardio-Vascular morbidity.

CONCLUSION

LV mass estimation and LVH diagnosis role in cardiovascular disease management is based on epidemiological research and also on clinical grounds. Despite more than 30 years of use echocardiography-based LVH calculation and definition are still variable among ultrasound technicians and laboratories around the world, leading to inconsistency among epidemiological studies and possibly limiting its clinical application. Several technical aspects of the echocardiographic exam can generate substantial errors in LV estimations, some of them equivalent in size to those expected to result from pathophysiological processes and therapeutic strategies. Also, adequate indexing for body size seems to be a critical point in defining pathological hypertrophy. LV mass is closely related to the other known cardiovascular risk factors, that must be taken into account concomitantly. Finally, since the risk associated to LV mass appears to be progressive, without a clear threshold, additional input

can be added at different baseline risks, defined by the prevalence of other known cardiovascular risk factors. The addition of multiple newer markers, however, leads to a small increment in risk stratification capacity over formulas applying only classical risk factors. Despite these limitations, the role of echocardiography in LV mass determination is of great clinical value. Considering all the aspects reviewed, use of echocardiography in clinical studies must be standardized applying already defined criteria. In delineating a study, if two-dimensional is impractical, then two-dimensional guided M-mode, using ASE criteria and Devereux modified formula, will allow estimation of LV mass with an acceptable level of accuracy.

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