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Original Research Article

LEFT VENTRICULAR DYSFUNCTION IN PREECLAMPTIC PATIENTS – ECHOGRAPHIC STUDY

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Abstract

Background: Preeclampsia is best described as a pregnancy specific syndrome that can affect virtually every organ system. Advancement in technology in the field of medicine like transthoracic echocardiography is the reference standard investigation for cardiovascular system diagnosis, monitoring and research purposes. The aim is to study the cardiac function in preeclamptic patients by transthoracic echocardiography and compare these features with normal pregnant patients, belonging to third trimester. **Materials and Methods:** The study was conducted from June 2018 to August 2019 at Department of Obstetrics and Gynaecology, KAPV Government Medical College, Trichy among 50 preeclampsia patients and 50 normotensive patients. Institutional Ethics Committee approval was obtained. Clinical history, Blood pressure, Ultrasonogram, Urine spot PCR for proteinuria, ECG, blood investigations and Echocardiography was done in all patients at third trimester. Data was entered in MS Excel and analysed using SPSS. Appropriate descriptive and inferential statistics were used, with p value <0.05 is considered statistically significant. **Result:** Age, Parity, Delivery, Weight, Height, BMI, Ejection fraction, Fractional shortening, Aortic root diameter, Left atrium diameter shows no statistically significant difference between the Groups. GA (Weeks), Blood pressure, Spot PCR, Birth weight, IVSs, IVSd, LVPWs, LVPWd, E Wave velocity, A Wave velocity, E/A ratio, IVRT shows highly statistically significant difference between the Groups. **Conclusion:** Blood pressure during pregnancy and postpartum showed a statistically significant drop in mid-pregnancy, followed by a progressive increase until term. The lack of the mid-trimester drop in blood pressure might play a predictive role for a subsequent development of early-onset preeclampsia. Women with established preeclampsia are characterised by a higher resistance in the entire arterial system. The altered arterial properties persisted after six months and were also elevated three years postpartum in women with previous preeclamptic pregnancy. These changes indicate that preeclampsia induces persistent cardiovascular disturbances.

INTRODUCTION

Pregnancy is the physiological change which causes dramatic and reversible changes in a woman's cardiovascular and hemodynamic system. All these changes are necessary for the fetus to develop normally. When this adaptation fails, the consequences of preeclampsia and other hypertensive disorders result which affects the growth of the fetus and delivery.[1,2]

Circulatory changes start early in pregnancy and reach peak levels towards the end of the second trimester. Cardiac physiology is affected by the increased levels of estrogens, prostaglandins and locally produced nitric oxide which decreases the systemic vascular resistance by 30 % and result in a mild decrease in blood pressure despite increase in cardiac output. Inspite of some compensating factors like decreased vascular resistance and low viscosity, pregnancy inevitably increases the effort of the heart. Therefore, if the cardiac status is carefully

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assessed between the 28th to 32nd week, one can make a reasonable estimate of how the heart will behave during labour.[1,2]

Preeclampsia is best described as a pregnancy specific syndrome that can affect virtually every organ system. In addition, it heralds a higher incidence of cardiovascular disease later in life. The cardiovascular system undergoes a host of changes in association with the development of preeclampsia, which ultimately lead to the classic low cardiac output - high systemic vascular resistant state.[3] Various societies provide different criteria for the diagnosis of preeclampsia. Common to all diagnostic criteria is that preeclampsia is a syndrome characterised by new-onset hypertension (140 mm Hg systolic blood pressure [SBP] or 90 mm Hg diastolic blood pressure [DBP]) on two occasions at least 4 hours apart arising after 20 weeks of gestation with proteinuria more than 300 mg per 24 hour urine collection with >1 organ system involvement and complete resolution within 12 weeks postpartum. Although not distinct entities, it is increasingly becoming apparent that early-onset preeclampsia is especially associated with poor placentation, fetal growth restriction, and worse long-term maternal cardiovascular outcomes than late-onset preeclampsia, whose pathogenesis is more related to predisposing cardiovascular or metabolic risks for endothelial dysfunction. Advancement in technology in the field of medicine like transthoracic echocardiography is the reference standard investigation for cardiovascular system diagnosis, monitoring and research purposes.[3-5]

It is a valid, precise and reproducible measurement device in research studies providing information not only about cardiac output, which the perioperative literature is currently focusing on, but also on other measurements of systolic function, and diastolic, structural and functional information of heart.

Aim & Objectives:

To study the cardiac function in preeclamptic patients by transthoracic echocardiography and compare these features with normal pregnant patients, belonging to third trimester.

MATERIALS AND METHODS

This was a Prospective cohort study conducted at the Department of Obstetrics and Gynaecology, KAPV Government Medical College, Trichy for the period of 15 Months [June 2018 to August 2019] among 50 preeclampsia patients and 50 normotensive patients. Institutional Ethics Committee approval was obtained.

Group 1: Normotensive pregnant patients - 50 cases, between age group of 18 to 32 years. Those pregnant women with normal blood pressure, Pregnant women in gestational age 28 to 40 weeks as calculated by LMP and dating scan, No previous h/o preeclampsia or essential hypertension and those who were not on treatment for any medical or surgical illness were included in the study. Pregnant women with previous history of hypertension (Recurrent gestational hypertension) and patients with medical disorders of pregnancy were excluded from the study. Group 2: Pregnant preeclamptic patients 50 cases, between age group of 18 to 32 years. Those pregnant patients with systolic BP >/=140mm Hg and diastolic BP>/=90mm Hg that develops after 20 weeks of gestation confirmed by repeated examination of at least 6 hours apart with proteinuria of trace to 2+ or spot PCR >0.3., Pregnant women in gestational age 28 to 40 weeks as calculated by LMP and dating scan, no previous H/O essential hypertension and no other medical disorders complicating this pregnancy were included in the study. Previous history of hypertension recurrent gestational hypertension and patients with medical disorders of pregnancy was excluded from the study. Both these groups of patients underwent echocardiography in third trimester to study the left ventricular function by using several parameters. This study also correlated mode of delivery and gestational age at the delivery and birth weight of fetus. Clinical history was recorded in detail about all patients. Blood pressure was measured using conventional sphygmomanometer, patient in sitting position, with the arm at the level of heart. Systolic BP and diastolic BP were measured using Korotkoff sound. Obstetric examination was performed. Ultrasonogram was performed for all patients and all the details are documented in two groups. Urine spot PCR for proteinuria was measured in two groups. ECG and other relevant blood investigations are performed in two groups. Echocardiography was done in all patients at third trimester. Echocardiography was performed in all patients in a left lateral recumbent position with 15 minutes undisturbed before echo. Two dimensional doppler echocardiography also performed using 3.5 MHz probe. M-mode studies were performed at the level of aorta, left atrium and LV at mid position between the tips of the mitral valve and papillary muscles. We recorded conventional grey scale cineloops, pulsed and continuous wave Doppler recordings of blood flow velocities, and tissue-Doppler cineloops of LV. The parameters measured were Systolic function - Left ventricular end-diastolic diameter (LVEDD), Left ventricular end-systolic diameter (LVESD), Ejection fraction (EF) was calculated by use of the Simpson's modified biplane method utilizing endocardial contours in the apical 4 and 2 chamber view and Fractional shortening (FS %). Diastolic function - Pulsed Doppler blood flow velocities were recorded at the mitral valve ring and tip, and in the LV outflow tract. Mitral peak early (E) diastolic flow velocity, Mitral peak late (A) diastolic flow velocity, E to A ratio (E/A RATIO) and Deceleration time. Data was entered in MS Excel. The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe the data descriptive statistics frequency analysis, percentage analysis were used for

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categorical variables and the mean & S.D was used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value .05 is considered as significant level.

RESULTS

A total of 100 subjects were recruited to the study divided into two groups. Group I served as normal subjects and Group II pre-eclamptic 50 subjects in each group. Age with Groups by Pearson's chi-squared test were $\chi 2=4.638$, $p=0.200>0.05$ which shows no statistical significant association between Age and Groups. Parity with Groups by Pearson's chi-squared test were $\chi 2=2.564$, $p=0.109>0.05$ which shows no statistical significant association between Parity and Groups. Delivery with Groups by Pearson's chi-squared test were $\chi 2=0.161$, $p=0.688>0.05$ which shows no statistical significant association between Delivery and Groups. [Table 1] Age/years with Groups by Unpaired t-test were t-value=0.765, $p=0.446>0.05$ which shows no statistical significant difference between Age/years and Groups. Weight/kgs with Groups by Unpaired t-test were t-value=0.348, $p=0.728>0.05$ which shows no statistical significant difference between Weight/kgs and Groups. Height/cm with Groups by Unpaired t-test were t-value=1.202, $p=0.232>0.05$ which shows no statistical significant difference between Height/cm and Groups. BMI with Groups by Unpaired t-test were t-value=0.460, $p=0.646>0.05$ which shows no statistical significant difference between BMI and Groups. GA (Weeks) with Groups by Unpaired t-test were t-value=11.188, $p=0.0005<0.01$ which shows highly statistical significant difference between GA (Weeks) and Groups. Blood Pressure with Groups by Unpaired t-test. In comparison of SBP with Groups were t- value=28.818, $p=0.0005<0.01$ which shows highly statistical significant difference between SBP and Groups similarly in comparison of DBP with Groups were t- value=20.676, $p=0.0005<0.01$ which shows highly statistical significant difference between SBP and Groups. Spot PCR with Groups by Unpaired t-test were t-value=13.689, $p=0.0005<0.01$ which shows highly statistical significant difference between Spot PCR and Groups. Birth weight with Groups by Unpaired t-test were t-value=7.143, $p=0.0005<0.01$ which shows highly statistical significant difference between Birth weight and Groups. IVSs with Groups by Unpaired t-test were t-value=4.590, $p=0.0005<0.01$ which shows highly statistical significant difference between IVSs and Groups. IVSd with Groups by Unpaired t-test were t-value=10.808, $p=0.0005<0.01$ which shows highly statistical significant difference between IVSd and Groups. LVPWs with Groups by Unpaired t-test were t-value=3.759, $p=0.0005<0.01$ which shows highly statistical significant difference between LVPWs and Groups. LVPWd with Groups by Unpaired t-test were t-value=1.755, $p=0.084>0.05$ which shows no statistical significant difference between LVPWd and Groups. Ejection fraction with Groups by Unpaired t-test were t- value=1.811, $p=0.074>0.05$ which shows no statistical significant difference between Ejection fraction and Groups. Fractional Shortening with Groups by Unpaired t-test were t- value=1.688, $p=0.096>0.05$ which shows no statistical significant difference between Fractional Shortening and Groups. E-wave velocity with Groups by Unpaired t-test were t-value=4.222, $p=0.0005<0.01$ which shows highly statistical significant difference between E-wave velocity and Groups. A-wave velocity with Groups by Unpaired t-test were t- value=3.032, $p=0.003<0.01$ which shows highly statistical significant difference between A-wave velocity and Groups. E/A Ratio with Groups by Unpaired t-test were t-value=5.028, $p=0.0005<0.01$ which shows highly statistical significant difference between E/A Ratio and Groups. IVRT with Groups by Unpaired t-test were t-value=3.412, $p=0.001<0.01$ which shows highly statistical significant difference between IVRT and Groups. Aortic root diameter with Groups by Unpaired t-test were t- value=0.281, $p=0.780>0.05$ which shows no statistical significant difference between Aortic root diameter and Groups. Left atrium diameter with Groups by Unpaired t-test were t- value=0.122, $p=0.904>0.05$ which shows no statistical significant difference between Left atrium diameter and Groups. [Table 2]

Table 1: Comparison of factors in each group

			Groups		Total	χ 2 - value	p- value
			Normal	Pre-Eclampsia			
Age	18 - 20 years	Count	7	8	15	4.638	0.200 #
		%	14.0%	16.0%	15.0%		
	21 - 25 years	Count	21	21	42		
		%	42.0%	42.0%	42.0%		
	26 - 30 years	Count	21	15	36		
		%	42.0%	30.0%	36.0%		
	31 - 35 years	Count	1	6	7		
		%	2.0%	12.0%	7.0%		
Parity	Multi	Count	30	22	52	2.564	0.109 #
		%	60.0%	44.0%	52.0%		
	Primi	Count	20	28	48		

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		%	40.0%	56.0%	48.0%		
Delivery	LSCS	Count	22	24	46	0.161	0.688 #
		%	44.0%	48.0%	46.0%		
	NVD	Count	28	26	54		
		%	56.0%	52.0%	54.0%		
# No Statistical Significance at p > 0.05 level							

Table 2: Comparison of factors between the groups

Variable	Groups	N	Mean	S.D	t- value	p- value
Age/years	Normal	50	24	3	0.765	0.446 #
	Pre Eclampsia	50	25	4		
Weight/kgs	Normal	50	67	12	0.348	0.728 #
	Pre Eclampsia	50	66	11		
Height/cm	Normal	50	153	8	1.202	0.232 #
	Pre Eclampsia	50	151	9		
BMI	Normal	50	29	5	0.460	0.646 #
	Pre Eclampsia	50	29	5		
GA (Weeks)	Normal	50	39	1	11.188	0.0005**
	Pre Eclampsia	50	36	2		
SBP	Normal	50	110.04	8.28	28.818	0.0005**
	Pre Eclampsia	50	149.20	4.88		
DBP	Normal	50	67.76	7.31	20.676	0.0005**
	Pre Eclampsia	50	93.20	4.71		
Spot PCR	Normal	50	0.27	0.05	13.689	0.0005**
	Pre Eclampsia	50	0.41	0.05		
Birth weight	Normal	50	2.96	0.29	7.143	0.0005**
	Pre Eclampsia	50	2.50	0.35		
IVSs	Normal	50	1.19	0.23	4.590	0.0005**
	Pre Eclampsia	50	1.02	0.10		
IVSd	Normal	50	1.07	0.20	10.808	0.0005**
	Pre Eclampsia	50	0.76	0.05		
LVPWs	Normal	50	1.31	0.22	3.759	0.0005**
	Pre Eclampsia	50	1.16	0.16		
LVPWd	Normal	50	0.99	0.14	1.755	0.084 #
	Pre Eclampsia	50	0.95	0.06		
Ejection fraction	Normal	50	64.22	6.61	1.811	0.074 #
	Pre Eclampsia	50	61.06	10.42		
Fractional Shortening	Normal	50	33.92	2.24	1.688	0.096 #
	Pre Eclampsia	50	35.02	4.03		
E-wave velocity	Normal	50	82.26	15.25	4.222	0.0005**
	Pre Eclampsia	50	70.84	11.55		
A-wave velocity	Normal	50	60.60	15.03	3.032	0.003**
	Pre Eclampsia	50	71.34	20.03		
E/A Ratio	Normal	50	1.41	0.35	5.028	0.0005**
	Pre Eclampsia	50	1.06	0.36		
IVRT	Normal	50	82.32	13.64	3.412	0.001**
	Pre Eclampsia	50	95.66	24.05		
Aortic root diameter	Normal	50	2.93	0.10	0.281	0.780 #
	Pre Eclampsia	50	2.92	0.17		
Left atrium diameter	Normal	50	3.14	0.15	0.122	0.904 #
	Pre Eclampsia	50	3.13	0.18		
# No Statistical Significance at p > 0.05 level ** Highly Statistical Significance at p < 0.01 level						

DISCUSSION

The cardiovascular system undergoes significant changes in preeclamptic patients compared to normal healthy women. In this study we have assessed the role of echocardiography and found it to be a useful technique for evaluation of maternal cardiac function in preeclamptic women. Rizwana et al. (2011) found that preeclampsia in women is characterized by high CO and a high vascular resistance state.[6]

Pregnancy represents a unique physiological condition in which heart undergoes morphological, hemodynamic, and functional adaptation with significant transient changes in cardiac loading conditions and work requirements. A thorough knowledge on maternal cardiac function during normal pregnancy is a prerequisite for identification of cardiac pathology in others. This is highly relevant since heart disease is one of the leading causes of non-obstetric mortality during pregnancy. In this thesis we studied the effects of hemodynamic changes during normal pregnancy on LV function by use of echocardiography and also hemodynamic changes and subclinical LV dysfunction in many preeclamptic patients.

Thus pregnancy is now considered a stress test to the maternal cardiovascular system. This study shows that women planning to become pregnant should be throughly screened for clinical and

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biochemical cardiovascular risk priorly and women presenting with clinical features of preeclampsia in pregnancy should be thoroughly investigated, and echocardiography should be done in all women, monitored periodically and treated according to recommendations.

Gilson et al. (1997) found no change in EF% and FS%, but the current study shows non-significant increase in circumferential fiber shortening, which is due to increase in myocardial contractility.[7]

Butters et al, reported that 67% of babies weighed less than the 10th percentile at birth after the mothers were treated for chronic hypertension.[8]

In our study also we found the above changes, and also that preeclampsia in an earlier stage may lead to premature delivery and there is a higher rate of low birth weight. One limitation of this study is that it was not possible to follow up subjects in the postpartum period.

This study shows that there are significant structural and functional changes in the cardiovascular hemodynamics in patients with preeclampsia. It appears that BP monitoring alone is insufficient to effectively identify the risk of cardiovascular complications in these women. Maternal echocardiography, if introduced into the routine management protocol, could help to identify women who are at high risk of developing complications.

Various etiological factors and hypothesis for pregnancy induced hypertension. The potential causes of pregnancy induced hypertension are Abnormal placentation (Steegerset al., 2010), Vasculopathy and inflammatory changes, Immunological factors, Genetic factors and Nutritional factors (Amir et al.,1998).[9,10]

According to Furuya et al., 2008 the spiral arterioles of the placental bed undergo a series of physiological changes. These arterioles are invaded by trophoblast, which breaks down the endothelium, internal elastic lamina and muscular coat of the vessel, which is converted to fibrinoid layer in endothelium. These changes occurs in two phases, the invasion of decidual segments of spiral arterioles in the first trimester and myometrial segments, by a subsequent in the second trimester, second phase occurs.

These physiological changes convert the vessels supplying the placenta from muscular end arteries to wide mouth sinusoids, which are unresponsive to vasoactive substances and transformed into low pressure high flow system to meet the needs of the fetus and placenta.

According to Granger et al., 2001a; Furuyaet al., 2008 in GHTN, there is inadequate maternal vascular response to placentation, and the primary invasion of trophoblast is partially impaired, and second phase of trophoblastic invasion fails to occur. This restriction of normal physiological changes, result in restricted placental flow, which becomes more severe with advancing gestation. Spiral arterioles show changes like endothelial damage, insudation of plasma constituents into vessel wall, proliferation of lipid laden myointimal cells and medial necrosis termed acute atherosis. Obstruction of lumen by atherosis may impair placental blood flow. These changes pathologically decrease placental blood flow and lead to infarcts, patchy necrosis and intracellular damage to the synctiotrophoblast and obliterative endarteritis of fetal stem arteries finally leads to incomplete development of fetal macrovascular system in pregnancy induced hypertension associated with fetal growth restriction.[11,12]

Granger et al., 2001b says in response to ischemic changes, various noxious substances are released from the placenta and decidua, these are mediators to provoke endothelial injury.(12) Cytokines such as (TNF-alpha) and interleukins contribute to the oxidative stress characterized by formation of reactive oxygen species (ROS) and free radicals that lead to formation of lipid peroxides. These free radical will damage endothelial cells, modify their nitric oxide production and interfere with prostaglandin balance. Oxidative stress also causes production of lipid laden macrophages foam cells seen in atherosis, activation of micro vascular coagulation seen in thrombocytopenia and increased capillary permeability seen in edema and proteinuria. According to Chen etal.,1993, 1994. Immunological factors also plays crucial role in the development of preeclampsia.[13] This factor include absence of blocking antibodies, decreased cell mediated immunity, involvement of cytokines and activation of neutrophils. An aberrant immune reaction between fetal trophoblast with maternal tissue in the placental bed is a fundamental factor in the etiology of preeclampsia,which often complicates first pregnancy. Incidence is also increased when multiple partners and in a subsequent pregnancy after birth control methods. Women who develop PIH have decreased proportion of helper T cells (Th 1) in early second trimester, compared with normotensive individuals. The Th 1/Th 2 imbalance may be mediated by adenosine, found in higher concentration in pregnancy induced hypertension women. The helper lymphocytes secrete cytokines that promote implantation and their dysfunction may leads to pregnancy induced hypertension.

By Haram et al., 2000; Nilsson et al., 2004 Familial predisposition for preelampsia has been recognized, single gene model and polygenic inheritance has been suggested.[14,15] In one swedish study, 60% concordance in monozygotic female twin pairs has been reported . It is also reported a HLA-DR4 association with proteinuria in pregnancy induced hypertension. A number of single gene mutation and inherited thrombophilia's may predispose to pregnancy induced hypertension. Polymorphisms of the genes for TNF, lymphotoxin- alpha and interleukin-1 have been studied with varying results.

Many research shown that relationship between dietary deficiencies and incidence of preelampsia. A diet high in fruits and green leafy vegetables that

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have antioxidant activity is associated with decrease in the incidence of pregnancy induced hypertension. Antioxidants enzymes and antioxidant nutrients, including carotenoids, alpha- tocopherol and thiols are the primary defence against oxidative stress and free radical induced damage. Antioxidants protect against free radical damage and oxidative stress to endothelium by their quenching abilities. When there is deficiency of nutrients and antioxidant protective mechanisms, there is increase in production of lipid peroxidation. This imbalance leads to oxidative stress and tissue injury (Palan et al.,2001).[16]

Sagol et al., 1999 states protective antioxidant systems are deficient in pregnancy induced hypertension and low maternal serum carotenoid level such as þ carotenes; lycopene and canthaxanthin have been observed in pregnancy induced hypertension.[17] Vitamin C and Vitamin E supplementation between 16 to 22 weeks gestation decreases the incidence of pregnancy induced hypertension by more than 50% (Chappell et al.,1999).[18]

By Haram et al., 2000; Preeclampsia is characterized by vasospasm, endothelial cell damage resulting in activation of coagulation system.[14]

A decrease in synthesis of nitric oxide (NO) and an increase in endothelin by the vascular endothelium in pregnancy induced hypertension could account for characteristic vasospasm which causes resistance and subsequent hypertension. Endothelial injury causes interstitial leakage through which blood constituents, including activated platelets and fibrinogen are deposited sub endothelially, resulting in diminished blood flow because of maldistribution; this ischemia of surrounding tissues would lead to necrosis, haemorrhage and other end organ disturbances characteristic of PIH.

Various noxious placental cytokines andfree radicals generated by oxidative stress after ischemia of placenta cause activation and dysfunction of vascular endothelium. This Intact vascular endothelium decreases responsiveness to nitric oxide (NO) and to anticoagulant properties. Any injury or activation of endothelium secretes substances which promote coagulation and increased sensitivity to vasopressors. Increased circulating fibronectin, factor VII antigen and thrombomodulin, all markers of endothelial dysfunction are reported in pregnancy induced hypertension/preeclampsia (Granger et al.,2001b).[12]

Normal pregnant women are refractory to vasopressors like angiotensin II. However women with pregnancy induced hypertension/preeclampsia have increased vascular reactivity to angiotensin II. This increased sensitivity precedes the onset of hypertension. Autoantibodies are thought to activate AT1 receptors and increased angiotensin II sensitivity. Up regulation of bradykinin receptors (B2) leads to heterodimerisation with angiotensin II type I receptors (ATI). ATI/B2 receptors have been shown to increase responsiveness to angiotensin IIin-vitro.

Endothelial prostacyclin (PGI_2), a vasodilator; its production is decreased in pregnancy induced hypertension/preeclampsia mediated by phospholipase A_2. Thromboxane A_2 (vasoconstrictor and platelet aggregator) levels are increased. Imbalance of prostaglandins, especially decreased prostacyclin: Thromboxane A_2 ratio, result in vasoconstriction and hypertension. In normal pregnancy, PGI_2 is more than TXA_2=Vasodilation=No hypertension. In Preeclampsia, PGI_2 is less than TXA_2=Vasoconstriction=hypertension (Chen et al.,1993).[13]

Vascular endothelial growth factors (VEGF) and placental growth factor are endothelial specific growth factors plays a crucial role in promoting angiogenesis; Activity of VEGF is mediated by interaction with two high affinity receptor tyrosine kinases: Kinase insert domain region (KDR) and fms like tyrosine kinase-1 (flt-1).These are expressed an endothelial surface. Alternative splicing of flt-1 results in over production of sflt-1; this leads to loss of attachment to cell membranes and is secreted in to the maternal blood. This will antagonize VEGF and PLGF by binding to it and preventing its interaction with endogenous receptors. Excess sflt-1 production is seen in pregnancy induced hypertension/pre-eclampsia placentas, which creates an antiangiogenic state and plays a causal role in the pathogenesis of maternal syndrome in pregnancy induced hypertension/pre eclampsia. PLGF is important in vasculogenesis and control of microvascular permeability (Wang et al., 2009).[19]

As explained above, pregnancy is hemodynamically characterized by increased blood volume, plasma volume ,cardiac output and heart rate, as well as a decrease in blood pressure and peripheral vascular resistance. However, preeclampsia, an entity with significant fetal risk, maternal morbidity and mortality, is characterized by high blood pressure and less vasodilatation than that observed in normal pregnancy. Pathology shows that the systemic arteries of preeclamptic women are significantly stiffer than observed in healthy pregnant women at term, and moreover, that this phenomenon persists 6 months postpartum, according to various study reports.

Cardiovascular diseases like hypertension and hypercholesterolemia, diabetes increase with advancing age and it is associated with ventricular and arterial stiffening. The changes in characteristic impedance and compliance we observed in patients with preeclampsia bears a similarity to patients as a result of aging, hypertension, and arteriosclerosis. Hence, our results provide further insight into the pathophysiological basis for the increased risk of cardiovascular events in women with previous

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history of hypertension and previous h/o preeclampsia.

The changes in circulating blood volume, plasma volume and cardiac output and changes in blood pressure, peripheral vascular resistance, compliance, myocardial function, heart rate and the neurohormonal system, all allow the cardiovascular system to meet the increased metabolic demands during pregnancy.

This thesis shows that we non-invasive echocardiographic evaluation of left ventricle combined with good clinical history and relevant blood investigations add important information on the interaction of the heart with systemic vasculature in patients susceptible for gestational cardiovascular disorders like preeclampsia, hypertension and peripartum cardiomyopathy.

Furthermore, maternal hemodynamic variables also influence fetal growth and thereby current and future health of the newborn. Finally, hemodynamic monitoring during pregnancy may add to the current risk stratification tools in terms of predicting future cardiovascular disease to the respective patient. Insight into the mechanisms of physiological changes in normal pregnancy is essential in follow up of pregnant women with maternal structural heart disease like congenital heart diseases and other valvular and ischemic heart diseases during pregnancy.

CONCLUSION

During normal pregnancy, profound alterations in LV function occur. Increases in circulating blood volume are reflected by increased CO and cardiac dimensions. LV contractility is significantly reduced, whereas filling pressures are unchanged. These findings suggest that pregnancy represents a larger load on the cardiovascular system than previously assumed. Reference values obtained are relevant in order to identify cardiovascular dysfunction in pregnant women with heart disease. During normal pregnancy there is an increase in cardiac output and decrease in blood pressure and peripheral arterial resistance whereas central aortic properties are less altered. The increased ventriculoarterial coupling index ($E_aI/E_{LV}I$) during normal pregnancy indicates a decrease in LV function not fully compensated for by vascular adaptation.

Blood pressure measured repeatedly by two different noninvasive devices during pregnancy and postpartum showed a statistically significant drop in mid-pregnancy, followed by a progressive increase until term. The lack of the mid-trimester drop in blood pressure might play a predictive role for a subsequent development of early-onset preeclampsia. Women with established preeclampsia are characterised by a higher resistance in the entire arterial system. The altered arterial properties persisted after six months and were also elevated three years postpartum in women with previous preeclamptic pregnancy. These changes indicate that preeclampsia induces persistent cardiovascular disturbances.

Limitations

Preconceptional data would be the preferred reference measurements for assessing hemodynamic alterations during pregnancy, since we know that the major changes occurs during the first 12 weeks of pregnancy is not obtained.

We didn't follow the patients during post-partum period and repeat follow up echocardiographic monitoring. To assess the period when the preeclamptic patients with high hemodynamic alterations and morphology of heart, return to baseline is not done.

Oral and hormonal contraceptives during preconceptional usuage and post-partum period might have influence on hemodynamic variations and pathology of preeclampsia and unfortunately we lack information. Furthermore, we do not have access to pregestational data like socio economic status and living conditons and dietary in any of the study groups, which describes any inference of cause-effect relationship between development of preeclampsia and persisting hypertension in previous preeclamptic women.

Longitudinal data during pregnancy in preeclamptic women would be preferable rather than single third trimester echo in order to detect hemodynamic changes very early in pregnancy that may be present before preeclampsia becomes clinically overt and which ones that occurs after clinical manifestation of the disorder.

Furthermore, studies of larger size than this, would make it possible to study hemodynamic changes in subgroups of preeclamptic women like those with early and late onset preeclampsia, mild and severe preeclampsia with or without fetal growth restriction and with or without pre-existing metabolic disorders like diabetes and metabolic syndrome.

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