Int J Biol Med Res. 2012; 3(1): 1289-1293

BioMedSciDirect Publications

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

Hemodynamic changes in normal Indian primigravida: Serial evaluation by echocardiography

Jyotsana R. Bharshankar [a*], Chaitali T. Kakade [b], Rajay N. Bharshankar [c] S, Ashok H. Kale [d].

[a] *Associate Professor, Department of Physiology, Indira Gandhi Government Medical College, Nagpur.*
[b] *Ex Junior resident, Dept of Physiology, Government Medical College, Nagpur*
[c] *Professor and Head, Dept of Physiology, Shree Guru Gobindsingh Tricentinary, Medical College, Hospital and Research Institute, Budhera, Gurgaon.*
[d] *Professor and Head, Dept of Physiology, Government Medical College, Nagpur*

ARTICLE INFO

Keywords:
Echocardiography;
Hemodynamic parameter;
Left Ventricular Systolic Function;
Primigravida

ABSTRACT

Aim: To evaluate the hemodynamic changes in normal Indian primigravida and to observe the onset, magnitude and recovery of these changes. **Method:** In a prospective study, 30 primigravid women were evaluated 4 times at early, mid and late gestation and at 6 weeks postpartum. At each visit, echocardiography was performed in the left lateral decubitus position to assess the hemodynamic changes. The data was subjected to statistical analysis to observe the changes at different gestational periods by using ANOVA. **Results:** Considering values of 6 weeks postpartum as baseline, the mean values of cardiac output (COP) increased in early gestational period (from 3.75±0.39 to 4.41±0.43 L/min, p<0.01). It continued to increase further in mid (4.95±0.5, p<0.001) and later gestational periods (5.57±0.56, p<0.001). Mean arterial pressure (MAP) was decreased in the early gestation (86.44±4.24 to 75.37±5.70 mm of Hg, p<0.001) and then increased. Total peripheral resistance (TPR) (dyne.sec.cm^{-5}) decreased in the early (1863.18±212 to1467.81±187,p<0.001), continued to decrease in mid gestation (1467.81±187 to 1228.09±115,p<0.001). Left ventricular mass increased gradually in early and mid gestation and the peak value was observed at late gestation. Ejection fraction and fractional shortening were same throughout pregnancy and at 6 weeks postpartum. **Conclusion**: The TPR and MAP decreases in the early, CO increases in the mid and later weeks of pregnancy. Left ventricular systolic functions were well preserved during pregnancy.

1. Introduction

Pregnancy is characterized by myriad of physiological changes of which the emergence of placenta and growing fetus is most dramatic. The hemodynamic readjustments occurring in pregnancy facilitate adaptations of cardiovascular system such as increase in blood volume, heart rate, cardiac output and decrease in total peripheral resistance.

In case of diversions from these readjustments, conditions like pre-eclampsia may predispose or previously unrecognized heart disorders may be unmasked. Cardiac output increases 30-40% from the pre-pregnancy levels [1,2]. However studies provide varying results as to the extent and timing of this increase. Particularly during the third trimester, reports on cardiac output diverge greatly [3]. Several hypotheses are postulated for the adaptive changes during pregnancy such as peripheral arterial vasodilatation hypothesis [4]. Renin-angiotensin system activation [5], sex hormone related mechanisms for sodium and fluid retention [6]. Concomitant increase in myocardial contractility may also contribute to increase in the cardiac output. [7]

In this regards, echocardiography is the most dependable means of assessment which is reliable reproducible and non-invasive technique suitable for pregnant women [8]. To the best of our knowledge such type of study was not being carried out particularly in Central Indian Population. So the current study was carried out with the aim to evaluate the changes in hemodynamic,

* Corresponding Author : Dr. Jyotsana R. Bharshankar
Associate Professor, Department of Physiology,
Indira Gandhi Government Medical College, Nagpur.
Mobile: 919822236661
Email: jyotsana.bharshankar@gmail.com

i. e. heart rate, cardiac output, mean arterial pressure, total peripheral resistance and left ventricular systolic functions in normal Indian primigravida in a prospective manner, find out the time of onset, magnitude of these changes. And to further explore the hypotheses of mechanisms responsible for cardiovascular adaptations unique to pregnancy.

2. Materials and Methods

The study protocol was approved by Institutional ethical committee of Government Medical College & Hospital Nagpur, Maharashtra state, India. The study period was from Dec 2007 to July 2009. The women attending antenatal outpatient department of Obstetrics were subjected to history and clinical examination.

2.1 Selection of subjects and initial assessments

Forty women having confirmed pregnancy and gestational age more than 12 weeks, normotensive primigravida in the age group of 20-30 years were selected. Women having history of medical illness, such as hypertension, heart disease, renal problems, diabetes mellitus, tuberculosis, thyroid disorders and anemia were excluded. Also women having history of oral contraceptive consumption and treatment for primary infertility, habits of tobacco chewing, smoking and alcohol consumption were excluded.

After enrolment the study protocol of subsequent visits and the procedure during each visit was explained and women gave informed written consent. Obstetrician performed clinical and sonological examination for confirmation of gestational age, excluding those with fetal abnormalities and to confirm singleton pregnancy.

Height was measured in cm; weight was measured to the nearest Kg by using standard methods. All observations were done by single person. Body surface area was calculated by using the Du-bois formula. [9] -

$$BSA = (WEIGHT)^{0.425}(Kg) \times (HEIGHT)^{0.725}(cm) \times 0.007184$$

Blood pressure was recorded in right arm in lying down position by auscultatory method. Onset of tapping sound was taken as systolic and diastolic blood pressure was taken at the muffling of korotkoff sound. Three such measurements were recorded at the interval of 5 minutes and average was taken as a final reading. The mean arterial pressure was calculated by using the standard formula. [10]

$$MAP = \text{Diastolic B. P.} + 1/3\ (\text{Systolic} - \text{Diastolic B. P.})$$

2.2: Echocardiography assessments

During each visit echocardiography was performed by the cardiologist in the cardiology department. Each time the women rested in the left lateral decubitus position with assistance for not less than 10 minutes in the echo room. The assessments were done by the single observer using the equipment – PHILIPS ie 33 & S 5-1 Sector array transducer with pure wave crystal technology incorporating band width of 2 high performance transducers, eliminating the need of multiple transducer selection. The operating frequency range extended from 0.5 – 1 MHz. (PHILIPS Healthcare Philips electronics India Ltd Technopolis Knowledge park, Andheri E. Mumbai).

Initial conventional 2-dimentionally guided M - Mode recordings were done to assess the cardiac structure. A variable frequency faced array transducer was used. All the conventional acoustic windows were used and usual plane of view (parasternal long and short axes, apical 4 chamber view) were registered.

All the recordings were done as per the recommendations by Devereux et al [11] and American society of Echocardiography. [12] Left ventricular mass was calculated by using the standard formula. –

$$LV\ mass\ (gm) = 0.8\ \{1.04[(LVID + LVPW + IVST)^3 - (LVID)^3]\ \} + 0.6$$

Where, LVID-Left ventricular internal diameter, LVPW - Left ventricular posterior wall thickness, IVST–Interventricular septal thickness.

Left ventricular systolic function was assessed by measuring ejection fraction and fractional shortening.

$$\text{Ejection fraction (EF\%)} = \frac{\text{LV diastolic volume - LV systolic volume}}{\text{LV diastolic volume}}$$

$$\text{Fractional shortening (FS)} = \frac{\text{LV end diastolic diameter - LV end systolic diameter}}{\text{LV end diastolic diameter}}$$

Doppler Echocardiography was used to calculate the stroke volume. [3, 13]

Stroke volume (ml) = Left ventricular outflow tract area (m^2) x velocity time integral (mm^2). Simultaneously recorded electrocardiograph determined heart rate in beats per minute.

Cardiac output (L/min) = Stroke volume (L) x heart rate (beats/min)

Cardiac Index ($L/min/m^2$) = cardiac output (L/min)/ Body surface area (m^2)

Total peripheral resistance was calculated by using the formula[14,15,1]

$$TPR\ (dyne.sec.cm^{-5}) = MAP \times 80 / \text{Cardiac output}$$

2.3 Statistical Analysis

The data was analyzed with statistical software STATA–10.0. Sample size of 30 followed up four times, continuous variables were presented as mean + SD. Changes in parameters of each gestational period were compared by one-way analysis of variance (ANOVA) followed by Bonferroni's as post-hoc test. $P<0.05$ was considered as significant.

3. Results

The present study enrolled 40 women initially, 10 women dropped out during the study period (3 developed hypertension, 2 suffered chronic cough, 3 turned non-compliant and 2 suffered miscarriage). Ultimately the cohort of 30 women was followed up as per the protocol (table 1).

Table 1:Study protocol for hemodynamic evaluation in primigravid pregnant women (n=30)

Follow up visit	Gestational weeks	Gestational period
1	14-17 weeks	Early Second trimester
2	24-27 weeks	Late second trimester
3	30-33 weeks	Mid third trimester
4	-------	6 weeks post partum

As the women were enrolled at 14 – 17 weeks of pregnancy, their pre-pregnancy and early pregnancy data was not available. The values for all the parameters at visit 4 were considered as baseline values with the exception of left ventricular mass.

The significant gain in weight was observed in visit 2 and visit 3 which lead to significant increase in BSA (table 2)

TABLE 2. The anthropometric data of the study women.

Parameters	Antenatal Visits		Post partum visit	
	1	2	3	4
Weight (kg)	43.03±3.45	47.2±4.35*	51.7±4.26**	43.6±3.90
Height(cm)	149.9±4.7	149.9±4.72	149.9±4.72	149.9±4.72
BSA (m2)	21.32±0.06	1.37±0.06	1.41±0.06†	1.33±0.06

Data presented as Mean ± SD, n = 30

a) * - p < 0.01 – significant change from preceding gestation period
b) ** - p < 0.001 – Highly Significant change from preceding gestationalperiod
c) † - p< 0.001 - Significant change (Visit 4 vs visit 3)
By using ANOVA with Bon-Ferroni's as post hoc test

Table 3 provides detail result of hemodynamics in primigravida during various visits. Comparing the baseline postpartum values and those obtained in the late gestational period (visit 4 Vs visit 3) cardiac output was increased by 48% (from 3.75±0.39 to 5.57±0.56 L/min; p<0.001). This change was due to increase in both heart rate and stroke volume. Cardiac output was significantly increased even in the first visit and at this point of time significant increase in the heart rate (p<0.001) contributed more than the increase in the stroke volume (p<0.5) towards the gain in cardiac output. MAP decreased significantly (p<0.001) at visit 1 to remain nearly same at visit 2 and increased significantly in the later weeks of pregnancy (p<0.001). These changes in MAP were attributed to similar changes in systolic and diastolic blood pressure. The diastolic BP which decreased to the extent of 15% during the visit 1 as compared to the baseline value, further decreased in visit 2. It contributed more to keep the mean MAP steady in visit 2 than the systolic BP. The TPR dropped significantly (p<0.01) initially (visit 1 Vs visit 4). It continued to drop significantly (p<0.001) even in the visit 2 and 3. All hemodynamic parameters showed significant change from visit 3 to visit 4 suggesting recovery.

Left ventricular mass showed a constant increase in the values throughout pregnancy but not to the significant extent. It although started recovery at 6 weeks postpartum, the systolic functions of left ventricle did not show significant changes in mean values of fractional shortening and ejection fraction as depicted in table 3.

TABLE 3 Hemodynamic data of pregnant women at various visits.

Parameters	Visit 1	Visit 2	Visit 3	Visit 4
SBP (mm of Hg)	98.13 ± 6.91†	101.66 ± 6.86	106.66±5.46*	111.33±5.92*
DBP (mm of Hg)	64.5 ± 6.21†	62.5 ± 6.91	68.66± 4.34**	74.33 ± 4.68*
MAP (mm of Hg)	75.37 ± 5.70††	75.55 ± 6.25	81.33± 3.55**	86.44 ± 4.24*
SV (ml)	49 ± 4.69	55.06 ± 6.11	59.8 ± 6.08*	47.2 ± 5.5**
HR (b/min)	86.96 ± 4.87††	90.13 ± 4.36*	93.33± 3.09**	79.33± 3.86**
COP (L/min)	4.41 ± 0.43†	4.95 ± 0.50**	5.57 ± 0.56**	3.75 ± 0.39**
CI (L/min/m^2)	3.12 ± 0.33†	3.61 ± 0.34**	3.94 ± 0.40**	2.80 ± 0.29*
TPR(dyne.sec.cm^{-5})	1467.81±187††	1228.09±115**	1180.45 ±150	1863.18±212**
LV Mass (gm)	94.43 ± 22.77	102.7 ± 23.12	109 ± 22	99.8 ± 19.7*
FS %	34.58 ± 8.20	34.57 ± 7.98	34.17 ± 7.71	34.78 ± 7.64
Ejection fraction %	71.23 ± 7.63	73.83 ± 7.38	72.26 ± 8.23	70.8 ± 8.23

a) Data presented as absolute mean ± SD, n = 30

b) FS -Fractional Shortening

c) * - p < 0.01 & ** - p<0.001 – Highly significant and very HighlySignificant change as compared to previous visit

d) † - p < 0.01 & †† - p < 0.001 – Highly significant and very Highly Significant change as compared to 6 weeks postpartum (visit 4 vs visit 1).

By using ANOVA with Bon-Ferroni's as post hoc test

4. Discussion

The present study was designed as longitudinal follow up study to delineate the gradual adaptations in hemodynamics and left ventricular functions during the course of pregnancy and postpartum. Significant weight gain started in the mid pregnancy to peak in late gestational weeks. Body surface area (BSA) showed significant increase in the late pregnancy as compared to baseline value ($p<0.001$). Thus BSA gain was gradual initially but obvious in later gestational weeks. This goes in accordance with other workers but the mean values of anthropometry in our study were lower. [14,16,1] This may be because of the ethnic and racial differences in the study population.

The MAP decreased significantly in the early gestational period, settled in the mid and in the later gestational period it increased significantly. It recovered at 6 weeks postpartum significantly. Such trend was also observed by other workers.[17,1,18,19,20] Though the systolic BP is comparatively increased in visit 2, the drop in diastolic BP in the early and mid pregnancy contributed more to keep MAP steady. In the late gestation MAP increased which was parallel with the gain in diastolic BP.

Various investigators have put forth the mechanisms behind these changes. Nitric oxide (NO), the vascular smooth muscle relaxing substance acts through cGMP mediated vasodilatation. The enzyme endothelium derived nitric oxide synthase (eNOS) is the key factor in its production. eNOS is biologically found in two isoforms i.e. ca++ dependent and ca++ independent. The activity of this ca++ dependent eNOS is increased by increase in the estradiol levels which are well documented in pregnancy [6]. Angiotensin II also stimulate NO production and thus it remains most important vasodilator during pregnancy [21,22]. Besides these there are other factors such as estrogen and progesterone metabolites (5-alpha dihydroprogesteron) which are present in high concentration in pregnancy enhances arterial refractoriness to angiotensin II. Increased secretions of ANP by heart in response to atrial distention contribute to vasodilatation. This is also mediated by cGMP on vascular smooth muscle. [23] In normotensive pregnancy vascular relaxation in peripheral artery and enhanced arterial compliance in conduit arteries has a crucial role in allowing the increased intravascular volume without increase in the blood pressure[24]. Total peripheral resistance in our study showed significant drop in visit 1, it even dropped further in visit 2. This observation supports the explanation quoted by other studies[24,25,26] .

Increase in the COP throughout pregnancy was observed to be significant in all visits. Similar trends were observed by many workers[1,7,14,18,20]. This enhancement in the COP was attributed to similar changes in HR and SV. Increase in the SV was significant in the visit 1. This seems to be secondary to the increased venous return by plasma volume expansion during pregnancy. Some authors suggest the mechanism behind volume gain to be activation of rennin angiotensin system (RAS) induced by arterial under filling due to primary peripheral vasodilatation.

It is thought to be an important factor modulating volume homeostasis and inducing volume expansion during pregnancy. [4,17,25] Note that values of TPR were significantly dropped in visit 1. Other studies observed this drop even before 14 weeks of pregnancy. [1,27]

Pregnancy induced peripheral arterial vasodilatation causes activation of atrial baroreceptors which further causes three major changes viz stimulation of the sympathetic system, activation of RAS and sodium retention, non osmotic vasopressin stimulation and water retention and thus effective blood volume is maintained.[4]

HR increases initially as a compensation for relative hypovolumia, in later weeks of pregnancy, high HR found to be necessary to circulate extra volume. [17] The raised levels of plasma T3 caused by estrogen induced increased TBG and thyrotrophic activity of HCG contributes to increase HR during pregnancy.

The mean values of COP obtained in our study are less than other studies with comparable techniques. This could be due to difference in study population involved. The maternal weight, height and body surface area are lower in Indian women than European, African and American countries. According to Hutchin's CJ the plasma volume expansion in European pregnant women was more than pregnant women of Indian origin with lesser maternal stature.[18] In another study, Ross P et al concluded that cardiac output in underweight pregnant women was lower than in normal weight pregnant women.[28]

When this COP is studied as a function of body surface area that is cardiac Index, the influence of maternal anthropometry is nullified and the observed values of cardiac index are similar to the other studies. [7,14,19]

The increased blood volume in pregnancy increases work load on left ventricle as evident rise in the LV mass. The cause is said to be same as heavy exercise causes skeletal muscle hypertrophy. [15] The values were comparable to those by other workers. The mean values of ejection fraction and fractional shortening in left ventricles did not show significant change in our study as observed by other workers. [1,7,8,24] Slight increase in the values may be because of the increase in the preload. [14] Besides this contractile functions of LV are also influenced by HR and after load. [29]

5. Conclusion:

Study shows a significant increase in COP at late second trimester maintained till third trimester. MAP, HR increased and

TPR decreased significantly in the early second trimester of pregnancy suggesting these changes might have started in the earlier weeks of pregnancy. Thus it supports the hypotheses suggested by previous studies. [4] The left ventricular systolic functions are not changed significantly. Further exploration is needed here for, is it the haemodynamic adaptations which are

well compensated? or some pregnancy related hormonal or metabolic changes are supporting the maintained left ventricular systolic functions.

The anthropometric parameters in Indian women were on lower side, so it affected the values of COP and TPR. Thus the data in our study may possibly represent the values of hemodynamic parameters in normal pregnant primigravid women of India.

Limitations

As a routine practice the women with 3 or more months of amenorrhea are referred to the Obstetric OPD and so the earlier hemodynamic status could not be assessed. Similarly the subsequent visits were planned according to their routine visits to the same departments in view of compliance. The evaluation in late third trimester also could not be done. Biochemical estimations of hormones related to mechanisms involved in hypervolemia could not be done because of financial constraints.

Acknowledgement:

We are thankful to the pregnant women who willingly participated in our study and also to the department of Cardiology, Super-specialty Hospital, Nagpur, India for the complete support.

6. References

[1] Mabie VC, DiSessa TG, Crocker LG, Sibai BM, Arheart KLA. Longitudinal study of cardiac output in normal pregnancy. Am J Obstet Gynecol 1994 March; 170 (3): 849-56

[2] Robson SC, Hunter S, Moore M and Dunlop W. Hemodynamic changes during purperium: A Doppler and M mode Echocardiographic study. Br J Obstet gynecol 1987; 94: 1028-1039.

[3] Van Oppen ACC, Stigter RH, Bruinse HW. Cardiac output in normal pregnancy: A critical review. Obstet Gynecol 1996; 87: 310-18.

[4] Schrier RW, Brier VA. Peripheral arterial vasodilation hypothesis of sodium and water retension; Implication for pathogenesis of preeclampsisa-eclampsisa. Obstet Gynecol. 1991; 77: 632-39.

[5] Maynard SE, Karumanchi SA, Thadani R. In Brenner and Rector Eds Hypertension and Kidney disease in pregnancy. The kidney Vol. 2, 8th ed. Saunders Eldevier.2004;1567-70

[6] Weiner CP, Lizasoain I, Baylis SA, Knowles RG, Charles IG. Induction of calcium dependent nitric oxide synthases by sex hormone. Proc Natl Acad Sci May 1994; 91: 5212-16.

[7] Katz R, Karliner JS, and Resnik R. Effects of natural volume overload state (Pregnancy) on left ventricular performance in normal human subjects. Circulation 1978; 58: 434-441.

[8] Robson SC, Hunter S, Boys RJ and Dunlop W. Serial study of factors influencing changes in cardiac output during human pregnancy. Am J Physiol 1989; 256: H1060-6D5.

[9] Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. Arch Intern Med 1916; 17: 863-71.

[10] Ganong WF. Review of Medical Physiology. 22nd edn. Mc Graw Hill. 2005: 571-72, 587, 598.

[11] Devereux RB, Casale PN, Eisenberg RR, Miller DH, Kligfield P. Electrocardiographic detection of left ventricular hypertrophy using echocardiographic determination of left ventricular mass as the reference standard. J Am Coll Cardiol. 1984; 3: 82-87.

[12] Sahn J, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiographic measurement. Circulation 1978; 58: 1072-83.

[13] Ihlen H, Amile JP, Dale J, Forfang K, Nitter-Hauge S, Otterstad JE, et al. Determination of cardiac output by Doppler echocardiography. Br. Heart J. 1984; 51: 54-60

[14] Desai DK, Moodley J, Naidoo DP, Echocardiographic assessment of cardiovascular hemodynamics in normal pregnancy. Obstetrics & Gynecology. July 2004; 104 (1): 20-29.

[15] Guyton AC, Hall GE. Textbook of Medical Physiology. 11th edn. New Delhi, India. Elsevier. 2007; 234, 235.

[16] Hutchin's CJ. Plasma volume-changes in pregnancy in Indian & European Primigravidae. Br J Obstet Gynecol. 1980; 87: 686-89.

[17] Duvekot JJ, Cheriex EC, Pieters FAA, Menheere Paul PCA, Peeters Louis LH. Early pregnancy changes in volume homeostasis develop as a consequence of preceding changes in maternal hemodynamic. Am Obstet Gynecol. 1993; 169 (6): 1382-1392.

[18] Gilson GJ, Samaan S, Crawford MH, Qualls CR, Curete LG. Changes in hemodynamics, ventricular remodelling, and ventricular contractility during normal pregnancy: A longitudinal study. Obstet Gynecol. 1997 Jun; 89 (6): 957-62.

[19] Simmons LA, Gillin AG, and Jeremy RW. Structural and functional changes in left ventricle during normotensive and preeclamptic pregnancy. Am J Physiol. 2002; 283: H1627-1633.

[20] Schannwell CM, Zimmerman T, Schneppenheim M, plehn G. Left ventricular hypertrophy and diastolic dysfunction in healthy pregnant women. Cardiology. 2002; 97: 73-78.

[21] Magness R, Rosenfeld C, Hassan A and shaul P. Endothelial vasodilator production by uterine and systematic arteries I. Effects of Ang II and PGI2 and NO in pregnancy. Am J. Physiol 1996; 270: 1914-1923

[22] Nathan L, Cuevas J, Chaudhari G. The role of nitric oxide in altered vascular reactivity of pregnancy in the rat. Br J Pharmacol. 1995; 114: 955-960.

[23] Cunningham FG, Leveno KJ, Bloom SL, et al. In Maternal Physiology. Williams Obstetrics 22nd edn. Mc Graw-Hill 2005; 129, 135-136.

[24] Poppas A, Shroff SG, Korcarz CE, Hibbard JU. Serial assessment of cardiovascular system in normal pregnancy. Circulation. 1997; 95: 2407-15.

[25] Carbillon L, Uzan M, Uzan S. pregnancy, vascular tone and maternal hemodynamics: A crucial adaptation. Obstet Gynecol Surv. 2000; 55: 574-81.

[26] Sala C, Campise M, Ambroso G, Motta T, Zanchetti A, Morganti A. Atrial natreuretic peptide and hemodynamic changes during normal human pregnancy. Hypertension 1995 April; 25 (4 Pt 1): 631-36.

[27] Mesa A, Jessurun C, Hernandez A, Adam K, Brown D,Vaughn WK and Wilansky S. Left ventricular diastolic function in normal human pregnancy. Circulation 1999; 99: 511-517.

[28] Rosso P, Donoso E, Braun S. hemodynamic changes in underweight pregnant women. Obstet Gynecol. 1992; 79: 908-12.

[29] Duvekot JJ, Peeters LL. Maternal cardiovascular hemodynamic adaptation to pregnancy. Obstet Gynecol Surrv 1994; 49 (12 Suppl): S1-14