ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Maternal Cardiopulmonary Adjustments in Pregnancy

***Seriki SA[1], Mfem CC[2], Oyama SE[3]**

[1]Department of Human Physiology, College of Medical Sciences, Edo State University, Uzairue, Nigeria

[2]Department of Human Physiology, College of Medical Sciences, University of Calabar, Calabar,Nigeria

[3]Department of Family Medicine, Alberta University, Canada

***Corresponding Author email: seriki.adinoyi@gmail.com; +2348036041121**

ABSTRACT

The major pregnancy-related hemodynamic changes include increased cardiac output, expanded blood volume, and reduced systemic vascular resistance and blood pressure. These changes contribute to optimal growth and development of the fetus and help to protect the mother from the risks of delivery, such as hemorrhage. A good knowledge of these cardiovascular adaptations is required to correctly interpret hemodynamic and cardiovascular tests in the gravida, to predict the effects of pregnancy on the woman with underlying cardiac disease, and to understand how the fetus will be affected by maternal cardiac disorders. The cardiovascular changes associated with normal pregnancy, and indeed a touch of the respiratory functions are reviewed here. The management of specific cardiac disorders, such as acquired and congenital heart diseases, heart failure, and arrhythmias, are also briefly discussed separately.

Keywords: hemodynamic changes, cardiac output, vascular resistance, expanded blood volume.

INTRODUCTION

The first measurement of cardiac output in a normal pregnant woman was performed by using a nitrous oxide technique, where it was found that there is an increase in cardiac output of approximately 50% during pregnancy [1]. It was however observed that late in pregnancy the cardiac output tends to decline toward non-pregnant levels, attributable to a decline in maternal physical activity [2].

The careful observations and measurements reported by researchers helped greatly to delineate many of the pregnancy-related hemodynamic changes [3]. Further studies revealed that changes in heart rate, blood pressure, venous pressure, and cardiac output may be responsible for the hemodynamic changes [4].

These changes persist throughout pregnancy and generally regress after delivery [5,6], however, there may not be a return to pre-pregnancy levels [7]. Invasive and non-invasive techniques have elucidated further the alterations in cardiovascular physiology during normal pregnancy.

Pregnancy-induced Changes

Cardiac Output

Cardiac output increases significantly (up to 50%) during pregnancy[8,9,10]. Results of several serial studies suggest that cardiac output rises significantly during the first trimester of pregnancy[10,11,12] and continues to rise through 26 to 34 weeks' gestation [9,13,14] , and is maintained at an elevated level to term if measured while the patient is in lateral recumbency [9,11]. The net result of these hemodynamic alterations is that early in pregnancy the increase in cardiac output at rest is accomplished predominantly through an increase in stroke volume.

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

As pregnancy advances, however, heart rate increases, and stroke volume decreases to non-pregnant levels; the increase in heart rate is responsible for maintaining the elevated cardiac output. A review of the changes in cardiac output during pregnancy suggests that cardiac output varies widely among individuals with singleton pregnancies in the third trimester [15], and the increase in cardiac output is even greater in a twin pregnancy [16,17].

A decline in cardiac output was however observed between 38 and 40 weeks' gestation for all positions studied (i.e., supine, sitting, and lateral recumbency), but the only statistically significant decline was encountered in the patients studied while supine. Doppler and echocardiographic studies have confirmed these changes in cardiac output [6,9]

Heart Rate

The rise in heart rate during pregnancy reaches 10 to 15 beats per min above non-pregnant values for most maternal positions [9].With the exception of the sitting position, the increase seems to be progressive until term.

Stroke Volume

Stroke volume is elevated to peak levels early in pregnancy (20 to 24 weeks' gestation) and progressively declines to non-pregnant levels at term. For the supine position, the stroke volume at term is 20 mL less than that measured 6 to 8 weeks postpartum [9].

Respiratory Function

Respiration includes the transfer of oxygen from the external air to the blood in the maternal pulmonary capillaries and oxygen consumption by the peripheral tissues. The maternal rate (including fetal) of oxygen consumption rises progressively during pregnancy, reaching a peak of 20% above non-pregnant levels [18]. The oxygen consumption of women at rest (but not basal) increases even more during pregnancy than does the basal value [19,20]. The total rate of maternal oxygen consumption in the pregnant woman is the sum of the rates of each of her tissues and that of the fetus and placenta. Approximately two thirds of the total increment in basal oxygen consumption during pregnancy is accounted for by the combined consumption of the fetus, placenta, and uterine muscle. The remaining increment is due to the increased oxygen requirements of the maternal myocardium, kidneys, muscles of ventilation, and mammary glands [20].

Also, the oxygen consumption is greater when measured in women with multiple gestations compared with singleton gestations [21]. The onset of labor is associated with a doubling in the average oxygen consumption and a threefold increase when measured during a uterine contraction [22]. The discrepancy between increases in cardiac output and oxygen consumption and the concomitant early fall in peripheral vascular resistance were compared with the hemodynamic changes of an arteriovenous fistula. From a teleologic standpoint, these alterations seem to anticipate reproductive needs because there is a rich flow of well-oxygenated blood to the uterus during early pregnancy when organogenesis is occurring and before fetoplacental circulation is fully developed. The arteriovenous oxygen difference widens to non-pregnant levels later in pregnancy [23].

Ventricular Function

The steroid hormones of pregnancy, particularly estrogen, not only affect vascular resistance, but also seem to have a direct effect on myocardial muscle. The mode of action is uncertain, but estrogens are structurally

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

similar to the cardiac glycosides. Estrogens may alter the actomyosin adenosine triphosphatase (ATPase) relationship in the myocardium, increasing myocardial contractility [24].

More recently, measurements of systolic time intervals have been performed in humans during the first and second trimesters [25].

The cause of reduction in pre-ejection period of left ventricular systole, particularly in the second trimester is unclear, but it could be due to a direct action of steroid hormones on myocardial cells [26]. Male transsexuals given high-dose estrogen therapy show increases in myocardial contractility [27].

Striking changes in cardiovascular function have been shown by echocardiographic studies during the course of normal pregnancy. Left ventricular diastolic dimension did not change, whereas there was a significant increase in left ventricular end-diastolic volume. The ventricular diameter-to-length ratio did not change, but the left ventricular posterior wall thickness increased with advancing gestation. The radius-to-wall thickness ratio decreased in mid-to-late gestation. No significant change occurred in left ventricular mass [28].

Previous research to evaluate indices of ventricular contractility did not find any significant changes in ejection fraction, fractional shortening, or velocity of circumferential fiber shortening. The rate-corrected ejection time and left ventricular wall stress were each less, as was the ratio of wall stress to velocity of circumferential fiber shortening (a load-independent assessment of left ventricular function). They concluded that independent of the increased preload and heart rate (reflected in velocity of circumferential fiber shortening) and of the decreased systolic blood pressure (reflected in wall stress), the intrinsic myocardial contractility was enhanced [28]. Other investigators studying a smaller number of patients found no change in ventricular contractility [29].

Vascular Resistance

Maternal vascular resistance decreases progressively throughout gestation [6]. This decline is similar to that of the decline in systolic and diastolic blood pressures [30]. Hypotheses for the cause of this vasodilation include decreased pressor responses to angiotensin II in pregnant women, increased vasodilatory prostaglandin synthesis, and alterations of extracellular matrix proteins in the vasculature. Nitric oxide (NO) has been studied intensively and is a frontrunner for this role [31,32]. NO is a short-lived molecule that is synthesized by NO synthase in the endothelium after stimulation and is released into the interstitium to exert its effect locally. In vascular smooth muscle, NO stimulates cyclic guanosine monophosphate (cGMP), which reduces cellular calcium concentrations and inhibits contraction. NO and cGMP have been found in increased concentrations in pregnant animals and can be reduced by the estrogen receptor antagonist tamoxifen, implying that estrogen modulates these increased levels of NO. Weiner and Thompson [32] hypothesized that the varying effects of pregnancy on vascular resistance in different organs could be due to differential levels of estrogen receptors on the endothelium.

The role of steroid hormones on NO levels has been elaborated by studies that have suggested a role of fetal dehydroepiandrosterone sulfate (DHEA-S) in maternal vasodilation [33,34]. DHEA-S is produced by the fetal adrenal gland and is metabolized by the placenta to estrogen, which then enters the maternal circulation. Pregnant women at term were infused with DHEA-S with monitoring of estrogen and nitrite levels. Nitrite levels doubled after DHEA-S infusion and peaked at 10 minutes after infusion. Estrogen levels increased fivefold and peaked at 60 minutes after infusion. The temporal relationship of the peak levels of nitrites and estrogen suggests that there may be other pathways involved in this process and that the fetus may play a role in regulating maternal blood pressure and volume through DHEA-S production. The statistical power of these studies is limited, however, by the small number of patients studied.

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Blood Volume

Blood volume, composed of plasma volume and red blood cell (RBC) mass, increases 20% to 100% during pregnancy [35,36]. The rise begins in the first trimester and continues throughout pregnancy but at a much slower rate during the third trimester [35,37,38]. The total increment seems to depend on several factors, including maternal weight [36] and the weight of the products of conception [36,39,40]. Expansion of the plasma volume (40% to 50%) is responsible for most of the increase in blood volume, especially between the 6th and the 24th weeks of pregnancy. Further minimal expansion occurs in the third trimester. Red Blood Cell mass increases progressively throughout pregnancy. The increment in total RBC volume ranges from 20% to 35% when compared with non-pregnant values [35]. The "physiologic anemia of pregnancy" results from the disproportionate expansion of plasma volume compared with RBC mass. The resulting hemodilutional anemia is maximal between 16 and 22 weeks of pregnancy, but hematocrit and hemoglobin values increase in the third trimester because the RBC mass continues to expand, whereas plasma volume increases only minimally [41]. Multiple gestation is associated with a greater expansion of the blood volume; however, the presence of a fetus is not required [35,42]. Even when iron stores are adequate and iron supplementation is provided, there is a decline in hemoglobin and hematocrit values late in pregnancy, but in some instances the fall is not statistically significant [18,43,44,45].

A report on the effect of posture on plasma volume late in pregnancy and consistently found a lower plasma volume in patients studied in the supine position than in patients in lateral recumbency. They attributed the findings to inferior vena caval occlusion, resulting in improper mixing of the dye (Evans blue) and extravasation of fluid into the lower extremities because of the elevated venous pressure [46].

Failure of the maternal blood volume to expand normally may be associated with suboptimal maternal and fetal outcomes, including impaired fetal growth [47,48], and may occur at 5 weeks' gestation [49]. Longo [50] hypothesized that the fetus may regulate the increment in maternal blood volume through the production of DHEA-S by the fetal adrenal gland. As described earlier, DHEA-S is the precursor of placental estrogens, which may play a role in vasodilation through NO production, triggering a compensatory expansion of blood volume through the renin-angiotensin-aldosterone axis. It has been shown that DHEA-S itself may play a role in this vasodilation [34].

Structural Alteration of Blood Vessels

The sudden appearance of spider angiomas during pregnancy is common, as is the occurrence of palmar erythema. Both of these events are thought to be hormonally mediated. Burwell and Metcalfe [51] reported the rapid growth of a pre-existing arteriovenous fistula during pregnancy. Rupture of splanchnic artery aneurysms is more common in women than in men before the age of 45. Most of these aneurysms rupture between the seventh and ninth months of pregnancy [52]. Rupture of cerebral aneurysms also have been reported to occur more frequently during pregnancy. The chance that a subarachnoid hemorrhage will occur increases with each trimester of pregnancy [53].

Histologic changes have been reported to occur in the wall of the aorta during pregnancy [54], but whether or not these are related to vessel strength and contribute to aortic dissection or rupture is open to question [55]. The exact mechanisms responsible for the many hemodynamic alterations associated with pregnancy are unclear, but undoubtedly many factors are involved. Neither the role played by the fetus nor that of the hypervolemia of pregnancy is known. From the data presented in the literature, the sex steroid hormones must play an important part. Observations by Ueland and Parer [56] that the intravenous infusion of natural estrogens in non-pregnant ewes produces an increase in cardiac output similar to that encountered in pregnancy in the same animals support this theory. Similarly the findings by Walters and Lim [57] of an

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

increase in cardiac output (15%) and in plasma volume (300 mL) in women taking oral contraceptives provide further evidence of the important role of the sex steroids.

Maternal Posture

Research findings have convincingly shown, by angiographic techniques, total occlusion of the inferior vena cava late in pregnancy in a patient in the supine position [58,59,60]. Other hemodynamic studies during pregnancy, using dye dilution techniques to estimate cardiac output, showed the effect of maternal posture [9,11]. Early in pregnancy (8 weeks) and up to 24 weeks' gestation, cardiac output remained essentially unchanged when measured in the supine and lateral positions. In both studies, there was a statistically significant decrease in cardiac output (25% to 30%) when measured in the supine position at 38 to 40 weeks' gestation. The decline was entirely attributable to a drop in stroke volume because heart rate remained relatively constant. Maternal upright positioning causes symptoms of syncope, however, in 8% of pregnant women in the first trimester of pregnancy. In the second trimester, the gravid uterus impairs venous return in standing women and can cause cardiovascular disturbances [61].

Using aortography, Bieniarz and co-workers [62] showed that the arterial side of the vascular tree also was affected to some degree by the large gravid uterus at term. They showed lateral displacement, attenuation, and elongation of the distal aorta as it was compressed against the maternal spine in supine recumbency. During hypotension, this effect becomes more pronounced.

Maternal Exercise

There is conflicting information in the literature regarding the maternal cardiorespiratory response to exercise. This controversy can be attributed in part to the different ways in which the patients were exercised, the maternal posture, and the techniques used to measure the hemodynamic response.

Standard treadmill exercise (weight bearing) is associated with higher rates of oxygen consumption in pregnant women than in women in the postpartum period [63]. A consistent increase in oxygen consumption has not been noted when non–weight-bearing exercise has been studied in pregnant women. In a serial study by Ueland and associates [9], the increment in cardiac output during mild, standardized, non–weight-bearing exercise on a bicycle ergometer was found to be the same throughout pregnancy and postpartum. Serial measurements of blood oxygen transport during exercise in this same group of patients [64] showed that exercise of mild intensity was associated with an increased oxygen requirement and cost more in terms of oxygen consumption during pregnancy. In contrast, slight decrease in oxygen consumption when a similar group of patients were studied in the pregnant and the non-pregnant state has been reported [63]. Metcalfe and colleagues [65] evaluated the effect of regular exercise before and during pregnancy and noted that neither the oxygen cost of steady-state exercise nor the oxygen debt incurred by exercise was elevated during pregnancy [66].

M-Mode echocardiography suggests that cardiac output increases secondary to increased fractional shortening early in pregnancy. Increase in left ventricular end-diastolic volume is the primary reason for increased cardiac output within pregnancy, however [67]. Bruce and Johnson [68] suggested that the decline in circulatory reserve is not related to impaired cardiac function but rather to peripheral pooling of blood resulting from the occlusion of the inferior vena cava by the uterus. There does not seem to be any appreciable buildup in oxygen debt during pregnancy when compared with non-pregnant controls.

The extent to which human uterine blood flow and oxygen consumption are altered by exercise during pregnancy is unclear. Studies considering the response of cardiac output to exercise suggest, however, that cardiac output is fixed and increases at a rate that parallels oxygen demand [12]. Animal data have shown

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

a reduction in uterine blood flow during exercise, accompanied by an increase in the maternal hematocrit. The augmented hemoglobin level enhances the blood oxygen-carrying capacity and serves to attenuate any possible reduction in oxygen delivery [69].

Fetal heart tracings that were obtained from women during recovery from moderately strenuous exercise revealed no evidence of fetal distress (although a consistent fetal tachycardia was noted). This group of women also had fetal non-stress tests before and after exercise. All tests were reactive, and there was no significant difference in the monitoring time required to obtain a reactive non-stress test before and after exercise [71]. The effect of exercise on the uterine artery blood flow velocity shows conflicting results with reports of no change and an increase and a decrease in systolic-to-diastolic ratios during maternal exercise.

CONCLUSION

With moderate exercise, the rise in cardiac output seems to be progressively smaller as pregnancy advances, suggesting a progressive decline in circulatory reserve. A similar small increment in cardiac output in response to exercise is found to occur late in pregnancy.

Additionally, blood flow is redistributed within the uterus, and the uptake of oxygen by the uterus as a whole, and by the fetus, remains constant. It is likely that fetal oxygen consumption is unaffected during mild-to-moderate exercise in human pregnancy as well.

This entire hemodynamic interplay of all factors discussed this review amounts to physiological way the body adjust cardiovascular functions to cope with pregnancy

REFERENCES

1 Lindhard J: über das Minutenvolum des Herzens bei Ruhe und bei Muskel-arbeit. Arch Physiol 161:233, 1915

2 Gammeltoft SA: Recherches sur le débit cardiaque par minute pendant la grossesse. Soc Biol 94:1099, 1926

3 Burwell CS: A comparison of the pressure in arm veins and femoral veins with specialreference to changes during pregnancy. Ann Intern Med 11:1305, 1938

4 Burwell CS, Strayhorn WD, Flickinger D, et al: Circulation during pregnancy. Arch Intern Med 62:979, 1938

5 Thornburg KL, Jacobson S, Giraud GD, Morton MJ: Hemodynamic changes in pregnancy. Semin Perinatol 24:11, 2000

6 Robson SC, Hunter S, Boys RJ, Dunlop W: Serial studies of factors influencing changes in cardiac output during human pregnancy. Am J Physiol 256:H1060, 1989

7 Clapp JF III, Capeless E: Cardiovascular function before, during, and after the first and subsequent pregnancies. Am J Cardiol 80:1469, 1997

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

8 Bader RA, Bader ME, Rose DJ, et al: Hemodynamics at rest and during exercise in normal pregnancy as studied by cardiac catheterization. J Clin Invest 34:1524, 1955

9 Ueland K, Novy MJ, Peterson EN, et al: Maternal cardiovascular dynamics: IV. The influence of gestational age on the maternal cardiovascular response to posture and exercise Am J Obstet Gynecol 104:856, 1969

10Walters WAW, MacGregor WG, Hills M: Cardiac output at rest during pregnancy and the puerperium. Clin Sci 30:1, 1966

11Lees MM, Taylor SH, Scott DB, et al: A study of cardiac output at rest throughout pregnancy. J Obstet Gynaecol Br Commonw 74:319, 1967

12de Schwarcz SB, Aramendia P, Taquini AC: Variaciones hemodinamicas en el embarazo normal. Medicina 24:113, 1964

13Adams JQ: Cardiovascular physiology in normal pregnancy: Studies with dye dilution technique. Am J Obstet Gynecol 67:741, 1954

14Roy SB, Malkani RP, Virik R, et al: Circulatory effects of pregnancy. Am J Obstet Gynecol 96:221, 1966

15vanOppen ACC, Stigter RH, Bruinse HW: Cardiac output in normal pregnancy: A critical review. Obstet Gynecol 87:310, 1996

16Crapo RO: Normal cardiopulmonary physiology during pregnancy. Clin Obstet Gynecol 39:3, 1996

17Hunter S, Robson SC: Adaptation of the maternal heart in pregnancy. Br Heart J 68:540, 1992

18Hytten FE, Leitch I: The Physiology of Human Pregnancy. p24, 2nd ed. Oxford, Blackwell Scientific Publications, 1971

19Pernoll ML, Metcalfe J, Schlenker TL, et al: Oxygen consumption at rest and during exercise in pregnancy. Respir Physiol 25:285, 1975

20Elkus R, Popovich J Jr: Respiratory physiology in pregnancy. Clin Chest Med 13:555, 1992

21Metcalfe J, Romney SL, Ramsey LH, et al: Estimation of uterine blood flow in normal human pregnancy at term. J Clin Invest 34:1632, 1955

22Wulf KH, Kunzel W, Lehmann V: Clinical aspects ofplacental gas exchange. In Longo LD, Bartels H (eds): Respiratory Gas Exchange and Blood Flow in the Placenta. p 505, Bethesda, MD, US Department of Health, Education, and Welfare, DHEW Publication No. (NIH) 73-3611972

23Burwell CS: Placenta as modified arteriovenous fistula, considered in relation to the circulatory adjustments to pregnancy. Am J Med Sci 195:1, 1938

24Csapo A: Actomyosin formation by estrogen action. Am J Physiol 162:406, 1950

25Burg JR, Dodek A, Kloster FE, et al: Alterations of systolic time intervals during pregnancy. Circulation 49:560, 1974

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

26Tanz RD: Inotropic effects of certain steroids upon heart muscle. Rev Can Biol 22:147, 1963

27Slater AJ, Gude N, Clarke IJ, et al: Haemodynamic changes and left ventricular performance during high-dose estrogen administration to male transsexuals. Br J Obstet Gynaecol 93:532, 1986

28Gilson GJ, Samaan S, Crawford MH, et al: Changes in hemodynamics, ventricular remodeling, and ventricular increases during normal pregnancy: A longitudinal study. Obstet Gynecol 89:957, 1997

29Geva T, Mauer MB, Striker L, et al: Effects of physiologic load of pregnancy on left ventricular decrease and remodeling. Am Heart J 133:53, 1997

30Villablanca AC: Heart disease during pregnancy: Which cardiovascular changes are normal or transient? Postgrad Med 104:183, 1998

31Poston L: Maternal vascular function in pregnancy. J Hum Hypertens 10:391, 1996

32Weiner C, Thompson L: Nitric oxide and pregnancy. Semin Perinatol 21:367, 1997

33Hata T, Ryukoh K, Fujiwaki R, et al: Effect of dehydroepiandrosterone sulfate on maternal cardiac function in term pregnancy. Am J Perinatol 13:11, 1996

34Manabe A, Hata T, Yanagihara T, et al: Nitric oxide synthesis is increased after dehydroepiandrosterone sulphate administration in term human pregnancy. Hum Reprod 14:2116, 1999

35Pritchard JA: Changes in the blood volume during pregnancy and delivery. Anesthesiology 26:393, 1965

36Ueland K: Maternal cardiovascular dynamics: VII. Intrapartum blood volume changes Am J Obstet Gynecol 126:671, 1976

37Chesley LC: Plasma and red cell volumes during pregnancy. Am J Obstet Gynecol 112:440, 1972

38Lund CJ, Donovan JC: Blood volume during pregnancy: Significance of plasma and red cell volume. Am J Obstet Gynecol 98:393, 1967

39Hytten FE, Paintin DB: Increase in plasma volume during normal pregnancy. J Obstet Gynaecol Br Commonw 70:402, 1963

40Rovinsky JJ, Jaffin H: Cardiovascular hemodynamics in pregnancy: 1. Blood and plasma volumes in multiple pregnancy Am J Obstet Gynecol 93:1, 1965

41Scott DE: Anemia in pregnancy. In Wynn RM (ed): Obstetrics and Gynecology Annual: 1972. p 219, New York, Appleton-Century-Crofts, 1972

42O'Day MP: Cardio-respiratory physiological adaptation of pregnancy. Semin Perinatol 21:268, 1997

43McFee JG: Anemia in pregnancy: A reappraisal. Obstet Gynecol Surv 28:769, 1973

44Chisholm M: A controlled clinical trial of prophylactic folic acid and iron in pregnancy. J Obstet Gynaecol Br Commonw 73:191, 1966

45Pritchard JA: Anemias complicating pregnancy and the puerperium. In Maternal Nutrition and the Course of Pregnancy. Committee on Maternal Nutrition/Food and Nutrition Board, National Research

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Council, National Academy of Sciences P 74, 1970

46Chesley LC, Duffus GM: Posture and apparent plasma volume in late pregnancy. J Obstet Gynaecol Br Commonw 78:406, 1971

47Croall J, Sherrif S, Matthews J: Nonpregnant maternal plasma volume and fetal growth retardation. Br J Obstet Gynaecol 85:90, 1978

48Goodlin RC, Quaife MA, Dirksen JW: The significance, diagnosis, and treatment of maternal hypovolemia as associated with fetal/maternal illness. Semin Perinatol 5:163, 1981

49Duvekot J, Cheriex E, Pieters F, et al: Maternal volume homeostasis in early pregnancy in relation to fetal growth restriction. Obstet Gynecol 85:361, 1995

50Longo LD: Maternal blood volume and cardiac output during pregnancy: A hypothesis of endocrinologic control. Am J Physiol 245:R720, 1983

51Burwell CS, Metcalfe J: Physiology and management. Heart Disease and Pregnancy. Boston, Little, Brown, 1958

52Abramovich DR, Francis W, Helsby CR: Two cases of ruptured aneurysm of splanchnic arteries in pregnancy with comment on the lesser sac syndrome. J Obstet Gynaecol Br Commonw 76:1037, 1969

53Donaldson JO: Neurology of Pregnancy. p 124, Philadelphia, WB Saunders, 1978

54Manalo-Estrella P, Barker AE: Histopathologic findings in human aortic media associated with pregnancy. Arch Pathol 83:336, 1967

55Cavanzo FJ, Taylor HB: Effect of pregnancy on human aorta and its relationship to dissecting aneurysms. Am J Obstet Gynecol 105:567, 1969

56Ueland K, Parer JT: Effects of estrogens on the cardiovascular system of the ewe. Am J Obstet Gynecol 96:400, 1966

57Walters WAW, Lim YL: Haemodynamic changes in women taking oral contraceptives. J Obstet Gynaecol Br Commonw 77:1007, 1970

58Howard BK, Goodson JH, Mengert WF: Supine hypotensive syndrome in late pregnancy. Obstet Gynecol 1:371, 1953

59Scott DB, Kerr MG: Inferior vena cava pressure in late pregnancy. J Obstet Gynaecol Br Commonw 70:1044, 1963

60Kerr MG, Scott DB, Samuel E: Studies of the inferior vena cava in late pregnancy. BMJ 1:532, 1964

61Schneider K-TM, Deckardt R: The implication of upright posture on pregnancy. J Perinatol Med 19:121, 1991

62Bieniarz J, Grottogini JJ, Curachet E, et al: Aortocaval compression by the uterus in late human pregnancy: II. An arteriographic study Am J Obstet Gynecol 100:203, 1968

63Knuttgen HG, Emerson K Jr: Physiological response to pregnancy at rest and during exercise. J Appl

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Physiol 36:549, 1974

64Ueland K, Novy MJ, Metcalfe J: Cardiorespiratory responses to pregnancy and exercise in normal women and patients with heart disease. Am J Obstet Gynecol 115:4, 1973

65Metcalfe J, McAnulty JH, Ueland K: The effects of pregnancy on the cardiovascular system and oxygentransport. Burwell and Metcalfe's Heart Disease and Pregnancy, Physiology and Management. 2nd ed.. Boston, Little, Brown, 1986

66Robbe H: Physical working capacity, blood volume and heart volume in cardiac patients during and after pregnancy. Acta Obstet Gynecol Scand 38:1, 1959

67Veille J-C: Maternal and fetal cardiovascular response to exercise during pregnancy. Semin Perinatol 20:250, 1996