



ECHOCARDIOGRAPHIC CHANGES IN PREGNANT PATIENTS ATTENDING RURAL TERTIARY CARE HOSPITAL-DBVPRMC, LONI.

Anaesthesiology

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ABSTRACT

During pregnancy, significant physiological adaptations support increased metabolic demands and fetal development, particularly affecting the cardiovascular, respiratory, hematological, and renal systems. Echocardiographic findings in pregnant women at a rural tertiary care hospital showed increased stroke volume (63.71 ± 5.16 mL vs. 55.0 ± 4.9 mL), cardiac output (5406.39 ± 684.78 mL/min vs. 4500 ± 600 mL/min), and left ventricular mass (168.11 ± 3.39 g vs. 140.0 ± 10.0 g), indicating cardiac remodeling. Pregnancy increases demand on the cardiovascular system, leading to significant adaptations, including higher cardiac output (CO), plasma volume, stroke volume (SV), and heart rate (HR), along with decreased systemic vascular resistance (SVR) and mean arterial pressure. Hemodynamic changes included elevated heart rate (84.79 ± 7.62 bpm vs. 75.00 ± 6.50 bpm) and systolic BP (120.84 ± 7.05 mmHg vs. 115.00 ± 6.80 mmHg), with lower diastolic BP and MAP. Doppler findings revealed reduced isovolumetric relaxation time and increased ejection time. These adaptations optimize maternal-fetal circulation but require careful anesthetic management, considering increased oxygen consumption, hypercoagulability, and altered drug sensitivity. Understanding these changes enhances obstetric and perioperative care.

KEYWORDS

Echocardiography, Physiological changes, Pregnancy

INTRODUCTION

During pregnancy, the body undergoes various anatomical and physiological changes to support the increased metabolic demands, facilitate the proper development of the fetus, and prepare for delivery. Surgical emergencies in pregnant women, such as ovarian cyst torsion, appendicitis, strangulated hernias, and severe trauma, demand immediate treatment.⁽¹⁾ Although the risk associated with surgery is comparable to that of the general population, managing anesthesia during this period is particularly challenging.⁽²⁾

Changes Related To Cardiovascular System

In early pregnancy, the increase in blood circulation is due to higher levels of estrogen and progesterone, leading to peripheral blood vessel dilation and a decrease in systemic vascular resistance (SVR).^(3,4) By the eighth week, cardiac output (CO) begins to rise to sustain blood pressure and support the uteroplacental unit, with an increase of 30-40% by the 24th week.^(5,6) Initially, there is a rise in stroke volume (SV),⁽⁷⁾ but subsequently, the heart rate (HR) increases to further elevate CO. The heart rate typically goes up by 15-25%, while stroke volume increases by 20-30%. Blood volume rises by as much as 2000 mL, which enhances preload and end-diastolic volume (EDV), aiding in the management of blood loss.⁽⁸⁾ A normal ECG during pregnancy may reveal left axis deviation, inverted T waves, and indications of left ventricular hypertrophy resulting from heart position changes and diaphragm elevation.⁽⁹⁾

Anaesthetic Implications⁽¹⁰⁾

Enlargement of the epidural venous plexus heightens the likelihood of a bloody tap and potential complications when placing an epidural catheter. Because of decreased sensitivity of adrenergic receptors, larger quantities of vasopressors such as phenylephrine are required to control hypotension. In cases of general anesthesia, diminished stroke volume and sympathetic blockade may exacerbate supine hypotensive syndrome, therefore it is advisable to avoid lying supine or to utilize a lateral wedge.

Changes In The Respiratory System

By the second trimester, there is a 45% rise in minute ventilation,

attributed mainly to an increase in tidal volume,⁽¹²⁾ which reaches 50% above pre-pregnancy levels by full term. The significant factor is a 40% upsurge in tidal volume, supplemented by a 15% increase in respiratory rate.⁽¹³⁾ Although alveolar ventilation also rises, flow volume loops do not change.⁽¹⁴⁾ During labor, minute ventilation can increase by 70-200%, while PaCO₂ decreases by 10-15 mmHg, and oxygen consumption increases by 40-75%. After giving birth, these physiological changes generally return to pre-pregnancy levels within 6-8 weeks.

Anaesthetic Implications

During pregnancy, the Mallampati classification worsens, especially during labor, increasing intubation difficulty due to airway changes, larger breasts, and obesity.⁽¹⁵⁾ Short-handled laryngoscopes, narrower tubes, and a ramp position may help, while nasotracheal intubation should be avoided due to bleeding risk. Reduced functional residual capacity (FRC) and increased oxygen consumption cause rapid desaturation during apnea.⁽¹⁶⁾ Elevated minute ventilation accelerates pre-oxygenation and anesthetic absorption. Preventing hyperventilation is crucial to avoid respiratory alkalosis and impaired fetal oxygen delivery. Epidural analgesia helps by reducing metabolic demands during labor.⁽¹⁷⁾

CHANGES IN THE HEMATOLOGICAL/IMMUNE SYSTEM

Leukocyte count increases to around 15,000/mm³, primarily due to polymorphonuclear cells with impaired function, heightening infection severity without increasing susceptibility.^(18, 19) Platelet production rises, but hemodilution and destruction prevent a significant increase, sometimes causing gestational thrombocytopenia, which resolves postpartum.⁽²⁰⁾ Pregnancy induces a hypercoagulable state, with increased clotting factors (except XI and XIII), reduced anticoagulants, and decreased fibrinolysis due to placental plasminogen activator inhibitor. Prothrombin and activated partial thromboplastin times decrease by 20%, with elevated fibrin degradation products and plasminogen levels.⁽²¹⁻²⁶⁾

Anaesthetic Implications

In a healthy pregnant woman, it is not required to check the platelet

count prior to neuraxial anesthesia or analgesia. Patients with severe preeclampsia face a heightened risk of developing epidural hematoma due to a significant decrease in platelets, and thus, it is essential to obtain a platelet count within six hours before inserting an epidural or removing a catheter. Nevertheless, it is prudent to assess both platelet count and function (aggregability).^(10,27)

CHANGES IN THE GASTROINTESTINAL SYSTEM

The expanding uterus displaces the stomach and weakens the lower esophageal sphincter (LES),⁽²⁸⁾ resulting in gastroesophageal reflux in as many as 80% of cases. Progesterone causes relaxation of the LES, reductions in esophageal peristalsis, and a delay in intestinal transit, leading to constipation. Gastric emptying is typically normal but slows down during labor and postpartum, with solid food potentially remaining in the stomach for as long as 18 hours.^(29,30) Elevated estrogen levels may lead to spider angiomas and palmar erythema, and more than half of pregnant women may develop esophageal varices,⁽³¹⁾ which typically resolve after labor.⁽³²⁾ Plasma dilution results in a 60% decrease in serum albumin, while serum cholinesterase levels drop by 33% after delivery.^(33,34)

Anaesthetic Implications

No changes are needed in the fasting recommendations; however, the use of opioids can slow gastric emptying, which raises the risk of aspiration due to elevated intra-abdominal pressure and diminished tone of the esophageal sphincter, particularly under general anesthesia. To mitigate these risks, it is advisable to prioritize neuraxial anesthesia techniques, implement aspiration prevention strategies, and conduct rapid sequence induction when general anesthesia is required.⁽³⁵⁾

CHANGES IN THE RENAL SYSTEM

During pregnancy, there is an increase in renal blood flow and glomerular filtration rate (GFR), which results in lower levels of serum creatinine and blood urea nitrogen, while the number of nephrons remains stable.⁽³⁶⁾ Both plasma osmolality and sodium concentrations decline, whereas urinary protein excretion increases, with any values exceeding 300 mg/day warranting further investigation.⁽³⁷⁾ Glucosuria and aminoaciduria may present due to compromised tubular function.⁽³⁸⁾ Common symptoms include increased urinary frequency, susceptibility to infections, incontinence, and nocturia, all of which typically resolve within 4 to 6 weeks after giving birth.⁽¹⁰⁾

Anaesthetic Implications

Because pregnant women typically have a lower normal serum creatinine range, even a slight increase in these values indicates a more significant decline in kidney function. Reduced albumin levels result in higher free concentrations of drugs that are usually highly protein-bound, including digoxin, midazolam, thiopentone sodium, and phenytoin.⁽³⁸⁾

CHANGES IN THE ENDOCRINE SYSTEM

In the first trimester, thyroid-stimulating hormone decreases before returning to normal levels, and there may be occurrences of subclinical thyroid dysfunction without harmful effects. Human placental lactogen diminishes insulin sensitivity, leading to higher blood sugar levels after meals and a greater risk of hypoglycemia and ketoacidosis during periods of fasting. The secretion of prolactin increases due to both placental lactogen and dopamine, while the levels of oxytocin rise by 30%, which helps reduce the stress response to avoid premature labor.^(39,40,41)

Anaesthetic Implications

General anaesthesia may obscure the indications and symptoms of hypoglycaemia, whereas neuraxial anaesthesia may cause increased haemodynamic instability in individuals with autonomic dysfunction due to diabetes mellitus or diabetic ketoacidosis.⁽¹⁰⁾

CHANGES IN THE CENTRAL AND PERIPHERAL NERVOUS SYSTEMS

During pregnancy, there is an increase in cerebral blood flow, a decrease in cerebrovascular resistance, and an increased permeability of the blood-brain barrier. The minimum alveolar concentration (MAC) decreases by 25-40%,⁽⁴²⁾ probably due to the effects of progesterone. Endorphin concentrations do not increase until the commencement of active labor, according to a few studies^(43, 44, 45) therefore, this cannot explain early MAC decline. Dilatation of the epidural venous plexus caused by inferior vena cava (IVC) compression,⁽¹⁰⁾ along with an increase in epidural fat and a reduction

in cerebrospinal fluid (CSF) volume, improves sensory blockade. While CSF pressure stays stable, it does rise during contractions.^(46,47)

Anaesthetic Implications

Throughout pregnancy, the minimum alveolar concentration can reduce by as much as 30%,⁽⁴⁸⁾ and the sensitivity to intravenous anesthetics enhances.⁽⁴⁹⁾ The doses of spinal local anesthetics are reduced by 25–40% as a result of anatomical changes and increased neuronal sensitivity caused by progesterone.⁽⁵⁰⁾ Pregnant women are at a higher risk of experiencing hypotension and hemodynamic instability associated with neuraxial anesthesia.

OBSERVATION & RESULTS

Table -1 Demographics Of Pregnant Females And Normal Reproductive-age Females

Demographics	Pregnant female (Mean ± SD)	Normal Reproductive-Age Female (Mean ± SD)
Age	23.40 ± 4.15	24.50 ± 3.80
Height	157.48 ± 4.65	158.00 ± 4.50
Weight	59.31 ± 5.19	55.00 ± 4.90
Gestational age	38.24 ± 1.57	N/A
BSA	1.59 ± 0.08	1.55 ± 0.07
BMI	23.91 ± 1.72	22.50 ± 1.60

Table -2 Hemodynamic Parameters Of Pregnant Females And Normal Reproductive-age Females

Hemodynamic Parameters	Pregnant Female (Mean ± SD)	Normal Reproductive-Age Female (Mean ± SD)
Pulse	84.79 ± 7.62	75.00 ± 6.50
Systolic BP	120.84 ± 7.05	115.00 ± 6.80
Diastolic BP	64.18 ± 6.29	70.00 ± 5.90
Map	83.07 ± 5.87	85.00 ± 5.50

Table -3 Echocardiographic Parameters Of Pregnant Females And Normal Reproductive-age Females

Echocardiographic parameters	Normal Pregnancy (Mean ± SD)	Normal Reproductive-Age Female (Mean ± SD)
LA	30.68 ± 3.17	30.5 ± 2.9
MAPSE	2.03 ± 16.65	2.2 ± 0.2
TAPSE	26.04 ± 3.03	25.5 ± 2.8
EPSS	6.76 ± 1.79	5.0 ± 1.5
LVOT	16.18 ± 1.22	18.0 ± 1.3
FS	39.53 ± 4.44	37.0 ± 3.8
LVEF	61.05 ± 3.09	62.0 ± 2.8
LA VOLUME	26.27 ± 1.72	24.5 ± 1.6
SV	63.71 ± 5.16	55.0 ± 4.9
CO	5406.39 ± 684.78	4500 ± 600
MVA	3.51 ± 0.36	3.45 ± 0.3
Iv MASS	168.11 ± 3.39	140.0 ± 10.0
LV mass index	105.72 ± 6.17	90.0 ± 5.2
SI= SV/BSA	40.06 ± 3.87	35.0 ± 3.2
MCOT	0.347 ± 0.025	0.35 ± 0.02
IVRT	0.081 ± 0.008	0.095 ± 0.007
LVET	0.260 ± 0.019	0.240 ± 0.02
PASP	17.13 ± 1.16	17.5 ± 1.0

DISCUSSION

The study highlights significant hemodynamic and echocardiographic changes in pregnant women and normal reproductive age females, reflecting physiological adaptations essential for maternal and fetal circulation. They had slightly lower mean age but similar height, with increased weight (59.31 ± 5.19 kg vs. 55.00 ± 4.90 kg), BSA (1.59 ± 0.08 m² vs. 1.55 ± 0.07 m²), and BMI (23.91 ± 1.72 kg/m² vs. 22.50 ± 1.60 kg/m²), reflecting physiological weight gain. The study focused on women in late pregnancy (mean gestational age: 38.24 ± 1.57 weeks). Hemodynamically, pregnant women had a higher pulse rate (84.79 ± 7.62 bpm vs. 75.00 ± 6.50 bpm) and systolic BP (120.84 ± 7.05 mmHg vs. 115.00 ± 6.80 mmHg), but lower diastolic BP (64.18 ± 6.29 mmHg vs. 70.00 ± 5.90 mmHg) and MAP (83.07 ± 5.87 mmHg vs. 85.00 ± 5.50 mmHg).

In this study, echocardiographic parameters of pregnant women and normal reproductive-age females were studied. The left atrial (LA) diameter was 30.68 ± 3.17 mm vs. 30.5 ± 2.9 mm, MAPSE was 2.03 ± 16.65 mm vs. 2.2 ± 0.2 mm, TAPSE was 26.04 ± 3.03 mm vs. 25.5 ± 2.8 mm, EPSS was 6.76 ± 1.79 mm vs. 5.0 ± 1.5 mm, and LVOT was 16.18 ± 1.22 mm vs. 18.0 ± 1.3 mm. Fractional shortening (FS) was 39.53 ±

4.44% vs. 37.0 ± 3.8%, left ventricular ejection fraction (LVEF) was 61.05 ± 3.09% vs. 62.0 ± 2.8%, left atrial volume was 26.27 ± 1.72 mL vs. 24.5 ± 1.6 mL, stroke volume (SV) was 63.71 ± 5.16 mL vs. 55.0 ± 4.9 mL, and cardiac output (CO) was 5406.39 ± 684.78 mL/min vs. 4500 ± 600 mL/min. SV, CO (and their indexes), and LVEF increased across trimesters. An increase in SV and CO was similar to the observation by Savu et al. (51) CO increased during pregnancy because of a higher SV in early pregnancy and a later increase in HR, whereas total vascular resistance decreased. However, Savu et al. did not find any significant change in LVEF. The mitral valve area (MVA) was 3.51 ± 0.36 cm² vs. 3.45 ± 0.3 cm², left ventricular mass was 168.11 ± 3.39 g vs. 140.0 ± 10.0 g, left ventricular mass index was 105.72 ± 6.17 g/m² vs. 90.0 ± 5.2 g/m², and stroke index (SI) was 40.06 ± 3.87 mL/m² vs. 35.0 ± 3.2 mL/m². Doppler parameters included myocardial contraction time (MCOT) at 0.347 ± 0.025 s vs. 0.35 ± 0.02 s, isovolumetric relaxation time (IVRT) at 0.081 ± 0.008 s vs. 0.095 ± 0.007 s, left ventricular ejection time (LVET) at 0.260 ± 0.019 s vs. 0.240 ± 0.02 s, and pulmonary artery systolic pressure (PASP) at 17.13 ± 1.16 mmHg vs. 17.5 ± 1.0 mmHg.

CONCLUSION

This study highlights key cardiovascular changes during pregnancy, including increased weight, gestational duration, and body surface area. Significant hemodynamic modifications were observed in pulse rate, blood pressure, and cardiac function. Doppler assessments revealed changes in heart relaxation and contraction. These adaptations support maternal and fetal well-being by meeting circulatory demands.

REFERENCES:

- Goodman, S. (2002). Anesthesia for nonobstetric surgery in the pregnant patient. *Semin Perinatol*, 26(2), 136–145.
- Bajwa, S. S., Bajwa, S., Kaur, J., Singh, A., Singh, A., & Parmar, S. (2012). Prevention of hypotension and prolongation of postoperative analgesia in emergency cesarean sections: A randomized study with intrathecal clonidine. *Int J Crit Illn Inj Sci*, 2(2), 63–69.
- Chang, A. (2004). *Obstetric Anaesthesia: Principles and practice*. Chestnut DH, 15–38.
- Gaiser, R. (2014). Physiologic changes of pregnancy. *Chestnut's Obstetric Anesthesia: Principles and Practice* 5th ed. 15–38.
- Bhatia, P., & Chhabra, S. (2018). Physiological and anatomical changes of pregnancy: Implications for anaesthesia. *Indian J Anaesth*, 62(9), 651–657.
- Mashini, I. S., Albazzaz, S. J., & Fadel, H. E. (1987). Serial noninvasive evaluation of cardiovascular hemodynamics during pregnancy. *Am J Obstet Gynecol*, 156(5), 1208–1213.
- Robson, S. C., Hunter, S., Boys, R. J., & Dunlop, W. (1989). Serial study of factors influencing changes in cardiac output during human pregnancy. *Am J Physiol*, 256(4), H1060–1065.
- Wong C. Analgesia and anaesthesia for labor and delivery 2004.
- Ciliberto, C., & Marx, G. (1998). Physiological changes associated with pregnancy. *Update Anaesth Issue*, 9, 1–3.
- Bhatia, P., & Chhabra, S. (2018). Physiological and anatomical changes of pregnancy: Implications for anaesthesia. *Indian Journal of Anaesthesia*, 62(9), 651–657. doi:10.4103/ijaa.458_18
- Gaiser, R., Chestnut, D. H., Wng, C. A., Tsen, L. C., Kee, N., Beilin, W. D., & Myhre, Y. (2014). Physiologic changes of pregnancy. In *Chestnut's Obstetric Anesthesia: Principles and Practice* (pp. 15–38). Philadelphia: Elsevier Saunders.
- Nelson-Piercy C. *Handbook of Obstetric Medicine* 2nd ed. 2002.
- Kodali, B.-S., Chandrasekhar, S., Bulich, L. N., Topulos, G. P., & Datta, S. (2008). Airway changes during labor and delivery. *Anesthesiology*, 108(3), 357–362. doi:10.1097/ALN.0b013e31816452d3
- McClelland, S. H., Bogod, D. G., & Hardman, J. G. (2008). Apnoea in pregnancy: an investigation using physiological modelling. *Anaesthesia*, 63(3), 264–269. doi:10.1111/j.1365-2044.2007.05347.x
- Hägerdal, M., Morgan, C. W., Sumner, A. E., & Gutsche, B. B. (1983). Minute ventilation and oxygen consumption during labor with epidural analgesia. *Anesthesiology*, 59(5), 425–427. doi:10.1097/0000542-198311000-00011
- Prowse, C. M., & Gaensler, E. A. (1965). Respiratory and acid-base changes during pregnancy. *Anesthesiology*, 26(4), 381–392.
- Grindheim, G., Toska, K., Estensen, M.-E., & Rosseland, L. A. (2012). Changes in pulmonary function during pregnancy: A longitudinal cohort study. *BJOG*, 119(1), 94–101.
- Stirrat, G. M. (1994). Pregnancy and immunity. *BMJ (Clinical Research Ed.)*, 308(6941), 1385–1386. doi:10.1136/bmj.308.6941.1385
- Burrows, R. F., & Kelton, J. G. (1988). Incidentally detected thrombocytopenia in healthy mothers and their infants. *The New England Journal of Medicine*, 319(3), 142–145. doi:10.1056/NEJM198807213190304
- Palmer, S. K., Zamudio, S., Coffin, C., Parker, S., Stamm, E., & Moore, L. G. (1992). Quantitative estimation of human uterine artery blood flow and pelvic blood flow redistribution in pregnancy. *Obstet Gynecol*, 80, 1000–1006.
- Thornton, P., & Douglas, J. (2010). Coagulation in pregnancy. *Best Pract Res Clin Obstet Gynaecol*, 24(3), 339–352.
- Burrows, R. F., & Kelton, J. G. (1990). Thrombocytopenia at delivery: A prospective survey of 6715 deliveries. *Am J Obstet Gynecol*, 162(3), 731–734.
- Frölich, M. A., Datta, S., & Corn, S. B. (1998). Thrombopoietin in normal pregnancy and preeclampsia. *Am J Obstet Gynecol*, 179(1), 100–104.
- Sharma, S. K., Philip, J., & Wiley, J. (1997). Thromboelastographic changes in healthy parturients and postpartum women. *Anesth Analg*, 85(1), 94–98.
- Gerbasi, F. R., Bottoms, S., Farag, A., & Mammen, E. (1990). Increased intravascular coagulation associated with pregnancy. *Obstet Gynecol*, 75(3), 385–389.
- Liu, J., Yuan, E., & Lee, L. (2012). Gestational age-specific reference intervals for routine haemostatic assays during normal pregnancy. *Clin Chim Acta*, 413(1–2), 258–261.
- Karlsson, O., Spörng, T., Hillarp, A., Jeppsson, A., & Hellgren, M. (2012). Prospective longitudinal study of thromboelastography and standard hemostatic laboratory tests in healthy women during normal pregnancy. *Anesthesia and Analgesia*, 115(4), 890–898. doi:10.1213/ANE.0b013e3182652a33
- Shah, S., Nathan, L., Singh, R., Fu, Y. S., & Chaudhuri, G. (2001). E 2 and not P 4 increases NO release from NANC nerves of the gastrointestinal tract: Implications in pregnancy. *Am J Physiol Regul Integr Comp Physiol*, 280(5), R1546–R1554.
- Whitehead, E. M., Smith, M., Dean, Y., & Sullivan, O. (1993). An evaluation of gastric emptying times in pregnancy and the puerperium. *Anaesthesia*, 48(1), 53–57.
- Carp, H., Jayaram, A., & Stoll, M. (1992). Ultrasound examination of the stomach contents of parturients. *Anesth Analg*, 74(5), 683–687.
- Alonso, G. (2006). Effect of pregnancy on pre-existing liver disease physiological changes during pregnancy. *Ann Hepatol*, 5(3), 184–186.
- Practice Guidelines for Obstetric Anesthesia. (2016). *Anesthesiology*, 124(2), 270–300. doi:10.1097/aln.0000000000000935
- Cheung, K. L., & Lafayette, R. A. (2013). Renal physiology of pregnancy. *Advances in Chronic Kidney Disease*, 20(3), 209–214. doi:10.1053/j.ackd.2013.01.012
- Airoldi, J., & Weinstein, L. (2007). Clinical significance of proteinuria in pregnancy. *Obstetrical & Gynecological Survey*, 62(2), 117–124. doi:10.1097/01.ogx.0000253301.55009.ac
- Paeck, M., & Scott, K. (2008). *Obstetric Anesthesia and Uncommon Disorders* 2nd ed. 249–257.
- Carter, J. (1990). Liver function in normal pregnancy. *Aust N Z J Obstet Gynaecol*, 30(4), 296–302.
- Pearson, J. F., & Davies, P. (1973). The effect of continuous lumbar epidural analgesia on the acid-base status of maternal arterial blood during the first stage of labour. *BJOG*, 80(3), 218–224.
- Gaiser, R., Chestnut, D. H., Wng, C. A., Tsen, L. C., Kee, N., Beilin, W. D., & Myhre, Y. (2014). Physiologic changes of pregnancy. In *Chestnut's Obstetric Anesthesia: Principles and Practice* (pp. 15–38). Philadelphia: Elsevier Saunders.
- Casey, B. M., Dashe, J. S., Wells, C. E., McIntire, D. D., Byrd, W., Leveno, K. J., & Cunningham, F. G. (2005). Subclinical hypothyroidism and pregnancy outcomes. *Obstetrics & Gynecology*, 105(2), 239–245. doi:10.1097/01.AOG.0000152345.99421.22
- Casey, B. M., Dashe, J. S., Wells, C. E., McIntire, D. D., Leveno, K. J., & Cunningham, F. G. (2006). Subclinical hyperthyroidism and pregnancy outcomes. *Obstetrics and Gynecology*, 107(2 Pt 1), 337–341. doi:10.1097/01.AOG.0000197991.64246.9a
- Scheithauer, B. W., Sano, T., Kovacs, K. T., Young, W. F., Jr, Ryan, N., & Randall, R. V. (1990). The pituitary gland in pregnancy: a clinicopathologic and immunohistochemical study of 69 cases. *Mayo Clinic Proceedings*. Mayo Clinic, 65(4), 461–474. doi:10.1016/s0025-6196(12)60946-x
- Palahniuk, R. J., Shnider, S. M., & Eger, E. I. (1974). Pregnancy decreases the requirement for inhaled anesthetic agents. *Anesthesiology*, 41(1), 82–83.
- Steinbrook, R. A., Carr, D. B., Datta, S., Naulty, J. S., Lee, C., & Fisher, J. (1982). Dissociation of plasma and cerebrospinal fluid beta-endorphin-like immunoreactivity levels during pregnancy and parturition. *Anesth Analg*, 61(11), 893–897.
- Datta, S., Migliozi, R. P., Flanagan, H. L., & Krieger, N. R. (1989). Chronically administered progesterone decreases halothane requirements in rabbits. *Anesth Analg*, 68(1), 46–50.
- Bromage, P. R. (1961). Continuous lumbar epidural analgesia for obstetrics. *Can Med Assoc J*, 85, 1136–1140.
- Chan, M. T., Mainland, P., & Gin, T. (1996). Minimum alveolar concentration of halothane and enflurane are decreased in early pregnancy. *Anesthesiology*, 85(4), 782–786. doi:10.1097/0000542-199610000-00013
- Christensen, J. H., Andreasen, F., & Jansen, J. A. (1981). Pharmacokinetics of thiopental in caesarian section. *Acta Anaesthesiologica Scandinavica*, 25(2), 174–179. doi:10.1111/j.1399-6576.1981.tb01632.x
- Savu, O., Jurcut, R., Giuscă, S., van Miegheem, T., Gussi, I., Popescu, B. A., ... Voigt, J.-U. (2012). Morphological and functional adaptation of the maternal heart during pregnancy. *Circulation. Cardiovascular Imaging*, 5(3), 289–297. doi:10.1161/CIRCIMAGING.111.970012
- Igarashi, T., Hirabayashi, Y., Shimizu, R., Saitoh, K., Fukuda, H., & Suzuki, H. (2000). The fiberoptic findings of the epidural space in pregnant women. *Anesthesiology*, 92(6), 1631–1636.
- Fagraeus, L., Urban, B. J., & Bromage, P. R. (1983). Spread of epidural analgesia in early pregnancy. *Anesthesiology*, 58(2), 184–186.
- Flanagan, H. L., Datta, S., Lambert, D. H., Gissen, A. J., & Covino, B. G. (1987). Effect of pregnancy on bupivacaine-induced conduction blockade in the isolated rabbit vagus nerve. *Anesth Analg*, 66, 123–126.