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Alterations in physiology and anatomy during pregnancy

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Pregnant women undergo profound anatomical and physiological changes so that they can cope with the increased physical and metabolic demands of their pregnancies. The cardiovascular, respiratory, haematological, renal, gastrointestinal and endocrine systems all undergo important physiological alterations and adaptations needed to allow development of the fetus and to allow the mother and fetus to survive the demands of childbirth. Such alterations in anatomy and physiology may cause difficulties in interpreting signs, symptoms, and biochemical investigations, making the clinical assessment of a pregnant woman inevitably confusing but challenging. Understanding these changes is important for every practicing obstetrician, as the pathological deviations from the normal physiological alterations may not be clear-cut until an adverse outcome has resulted. Only with a sound knowledge of the physiology and anatomy changes can the care of an obstetric parturient be safely optimized for a better maternal and fetal outcome.

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Introduction

Pregnant women undergo anatomical and physiological changes that are not only important for coping with the increased metabolic demands of the pregnancy, but also to meet the developmental needs of the fetus and to allow mother and fetus to survive the demands of childbirth. Understanding these changes is essential for all clinicians looking after pregnant women as clinical assessment of a pregnant woman can be confusing and challenging. In the context of the critically-ill pregnant women, this understanding becomes crucial as different modifications may then be required to optimize their treatment. As a result, modified early obstetric warning score charts (MEOWS charts) has been introduced in many units. These have been suggested to bring about timely recognition, treatment and referral of women who might develop a critical illness during or after pregnancy [1]. This review describes the anatomical and physiological adaptations of pregnancy, emphasizing the clinical implications.

Cardiovascular changes

Cardiac output is calculated as the product of stroke volume and heart rate.

Stroke volume is defined as the quantity of blood pumped into the aorta during each cardiac cycle and is dependent on preload and afterload. In pregnancy, the blood volume increases. This leads to an increase in the amount of blood returning to the heart (the preload). In addition, the afterload is reduced because of maternal vasodilatation. As a result, the stroke volume increases by 20–30% during pregnancy [2].

Maternal heart rate increases early in pregnancy, peaking and plateauing in the third trimester, during which rates are 15-20 beats per minute higher [2].

As a result of the increase in stroke volume and maternal heart rate, cardiac output increases by 30%–50% during pregnancy, rising from the non-pregnant value of 4.6 L/min to 8.7 L/min. As the magnitude of the rise in heart rate is lesser than that of the stroke volume, most of the increase in cardiac output results from the rise in stroke volume [2]. The increase in cardiac output, noted as early as 6 weeks' gestation, peaks in early to mid-third trimester, and is maintained until term [3–5].

Mean arterial blood pressure (MAP), defined as the average arterial pressure during a single cardiac cycle, is important for the perfusion of organs. MAP is directly proportional to cardiac output and systemic vascular resistance. Systemic vascular resistance is mediated by progesterone and nitric oxide both of which relaxes vascular smooth muscle. Nitric oxide is produced in the endothelium of blood vessels and its production is up-regulated by oestradiol during pregnancy [6]. Systemic vascular resistance declines during pregnancy reaching a nadir at around 20 weeks of gestation followed by a gradual rise until term [6]. Despite the drop in systemic vascular resistance, the MAP falls minimally during pregnancy as the decrease in systemic vascular resistance is matched in magnitude by the rise in cardiac output [5]. Systolic BP remains stable during pregnancy, whilst the diastolic BP decreases to a nadir at 28 weeks before rising again towards term [5].

The increase in cardiac output during pregnancy also increases pulmonary circulation but the pulmonary capillary wedge pressure is unchanged. Pulmonary vascular resistance, like systemic vascular resistance, is reduced [7]. The increase in plasma volume is accompanied by a decrease of plasma colloid osmotic pressure of 10–15% [7]. Consequently, the colloid osmotic pressure/pulmonary capillary wedge pressure gradient falls by 30%, increasing susceptibility to pulmonary oedema in pregnant women [7]. In conditions like pre-eclampsia in which the pulmonary vessels are more permeable, meticulous attention to fluid input and output is important to avert the complications of pulmonary oedema.

During pregnancy, the blood flow to uterus and placenta constitutes up to 25% of the cardiac output and is important for the development of the fetus. In addition, the blood flow to the skin, kidneys and breasts also increases. Hence, the increase in cardiac output in pregnancy is important for the mother to keep up with the increase in basal oxygen consumption [8]. Maternal cardiovascular conditions associated with cyanosis, hypoxia or a lower cardiac output, will reduce oxygenated blood flow to the developing fetus. This may increase the rate of fetal complications like intrauterine fetal growth restriction, miscarriage and prematurity.

The anatomy of the heart undergoes structural changes during pregnancy. The heart is pushed upwards and rotated forward with its left border laterally displaced. In addition, the ventricular wall muscle mass and the larger valvular annular diameters are increased [9]. The end-diastolic volume increases in pregnancy. The increase in ventricular mass and end-diastolic volume contributes to the increase in stroke volume [9]. However, the end-systolic volume and end-diastolic pressure remain unchanged, reflecting increased cardiac compliance. Although the pregnant heart is physiologically dilated during pregnancy, there is no decrease in ejection fraction.

Haemodynamic changes in women with multiple pregnancies are even more pronounced. The cardiac output in women with twin pregnancies is at least 20% higher than those with singleton pregnancies because of a greater stroke volume and heart rate. These women have greater left ventricular end-diastolic and end-systolic dimensions along with an increased left ventricular mass and ejection fraction [10].

In labour, further haemodynamic changes occur, with each uterine contraction causing the transfer of 300–500 mls of blood from the uterus to the general circulation [11]. As a result of this increase in maternal circulation, the preload increases, with a concomitant rise in stroke volume and hence cardiac output. Cardiac output increases by 15% in the first stage and 50% in the second stage of labour [11]. Uterine contractions further increase both systolic and diastolic BPs. In addition, pain and anxiety may increase sympathetic tone resulting in rise in blood pressure and heart rate. Epidural anaesthesia, an effective form of pain relief during labour, helps to limit the effect of pain and anxiety on the rise in blood pressure and heart rate during labour. Epidural anaesthesia is therefore recommended in women with cardiac conditions (with the exception of conditions with severe outflow tract obstruction, e.g., aortic stenosis) where large fluctuations in cardiac output are undesirable [12].

Just immediately following delivery, the well-contracted uterus, the relief of inferior vena cava obstruction from an emptied uterus, and the transfer of extravascular fluid into the intravascular spaces all contribute to increase venous return and stroke volume, resulting in a further 60% rise in cardiac output. Women with cardiovascular decompensation are therefore at risk of pulmonary oedema during the second stage of labour and the immediate post partum period [12].

The transient rise in cardiac output immediately after delivery is sustained for 1 hour, before cardiac output falls with a reduction in heart rate and stroke volume. A third of the decrease in cardiac output occurs within 2 weeks, although cardiac output may take up to 24 weeks to return to non-pregnant values. The fall in stroke volume is associated with significant decrease in left atrial and left ventricular end-diastolic dimensions, and left ventricular wall thickness. Blood pressure usually falls immediately after delivery, but may rise, reaching a peak on days 3–6 postpartum [13].

During pregnancy, the findings on cardiovascular examination of the mother may be altered. Peripheral oedema, mild tachycardia, jugular venous distension, and lateral displacement of the left ventricular apex are normal in pregnant women [14]. The fifth Korotkoff sound is better correlated to intra-arterial blood pressure and should be recorded instead of the fourth Korotkoff sound [15]. A louder first heart sound with exaggerated splitting and a third heart sound may be heard in pregnant women [14]. Systolic murmurs along the left sternum due to increased flow across the pulmonary and aortic valves may be present in more than 90% of pregnant women. A continuous murmur over the breast may also be heard over the second to fourth intercostal space [16]. ECG changes that are observed but are otherwise of no clinical significance include: sinus tachycardia, left axis deviation, ectopic beats, inverted or flattened T waves, and a Q wave in lead III [17].

The circulation haemodynamics in a pregnant woman are altered when she lies supine, particular after she enters the second trimester. In this position, the enlarged gravid uterus compresses on the inferior vena cava, impeding venous return to the heart. At the same time, the aorta is compressed significantly [18]. Therefore, the cardiac output falls significantly, resulting in a reduction of uterine and fetal perfusion [19]. A labouring mother should therefore be positioned in a left-lateral tilt. More importantly, emptying the uterus by delivering the fetus may be essential to ensure effective cardiopulmonary resuscitation of a mother in cardiac arrest. In such a situation, the aim of emptying the uterus is not to salvage the fetus, but rather, to relieve the aorto-caval compression that may hinder effective resuscitation [20]. Because of aorto-caval compression, blood pressure should not be measured with the mother in the supine position. Rather, blood pressure should be measured with the

mother sitting or lying on her side with a 30-degree tilt. The cuff should be of an adequate size as too small a cuff can cause an overestimation of blood pressure [21].

As discussed earlier, pregnant woman may have a lower blood pressure and a faster heart rate because of physiological changes. This may sometimes prevent physicians from recognizing an impending shock due to critical illness. In addition, because the pregnant woman has a 30% greater blood volume than a non-pregnant woman, a pregnant woman may lose up to 1500 mls of blood before any manifestation of clinical signs. In significant obstetric haemorrhage, the compensatory mechanism involves shutting down of blood flow to the fetoplacental unit. Blood loss in the mother may therefore be first reflected as fetal distress and fetal heart rate should be monitored to assess this. In addition, hypotension is a very late sign, developing only when significant blood loss has occurred. A rising heart rate is an early compensation for hypovolaemia, and a maternal heart rate greater than 100 beats/min should be considered sinister until proven otherwise [22].

Further alterations in maternal cardiovascular measures may present in complicated pregnancies. For example, in a pregnancy complicated by intrauterine growth restriction and pre-eclampsia, the mother may have a lower cardiac output and heart rate but higher vascular resistance [23].

Respiratory changes

During pregnancy, the anatomy of the upper respiratory airway undergoes numerous changes. In addition to a larger neck circumference [24], there is increasing oedema of the upper respiratory airway involving the pharynx and larynx [25]. Therefore, intubation in a pregnant woman can be difficult, and smaller endotracheal tubes may be needed [26]. In addition, the blood vessels in the nose undergo vasodilatation causing capillary engorgement. Consequently, nose bleeding, rhinitis and nasal congestion are common [27].

Because of the enlarging uterus and increasing abdominal pressure, the diaphragm is elevated 4 cm [28]. In addition, progesterone and relaxin cause ligaments connecting the ribs to the sternum to relax [29]. Consequently, the subcostal angle of the rib cage increases from 68.5 to 103.5 degrees [30]. In addition, the chest circumference increases by 5 to 7 cm because of increases in the anterior-posterior and transverse diameters of the chest of up to 2 cm [31]. Despite the larger chest circumference, chest wall compliance is lowered [32]. A lower chest wall compliance coupled with an elevated diaphragm results in a 5% decrease in total lung capacity [32]. Vital capacity, which is the maximum volume of gas expired after maximum inspiration, is unaltered.

The functional residual capacity, which is the volume of air remaining in the lungs upon normal passive exhalation, reduces by 10–25% [28]. Functional residual capacity comprises expiratory reserve volume and residual volume, both of which decrease during pregnancy. The expiratory reserve volume, the maximum volume of air that can be exhaled from end expiratory position, decreases 15–20% by 200-300 mls [28]. The residual volume, the volume of air remaining in the lungs after a maximal exhalation, decreases 20–25% by 200-400 mls [28]. The inspiratory capacity increases 5–10% by 200–350 mls [28]. The total lung capacity, which is the sum of functional residual capacity and inspiratory capacity, decrease minimally by 5% at term [28].

Oxygen consumption increases by 30% and the metabolic rate increases by 15% [33]. The increase in maternal oxygen consumption during pregnancy and the lower functional residual capacity mean that pregnant women have lower reserves of oxygen and are at greater susceptibility to become hypoxic. Additionally, airway oedema puts the mother at risk for potential intubation difficulties. Adequate pre-oxygenation is therefore important in pregnant women undergoing general anaesthesia [34].

Spirometry parameters remain unchanged in pregnancy [35]. There is no change in Forced Vital Capacity (FVC), the determination of the vital capacity from a maximally forced expiratory effort. There is also no effect on the FEV1, the volume that has been exhaled at the end of the first second of forced expiration. The ratio of FEV1 to FVC remains unchanged when comparing pregnant to non-pregnant women. The peak expiratory flow rate (PEFR) is also essentially unchanged. Therefore, abnormal spirometry results in pregnancy should be attributed to underlying respiratory disease and not to the pregnancy itself.

Tidal volume and respiratory rate increase in pregnancy. The tidal volume increases 30–50% from 500 to 700 ml [36] while respiratory rate increases slightly by 1–2 breaths per minute. As a result of the

increase in tidal volume and respiratory rate, minute ventilation (the amount of gas inhaled or exhaled from a person's lung in one minute, calculated by multiplying tidal volume and respiratory rate) increases 20–50% from 7.5 to 10.5 L/min. [36] Hyperventilation is caused by progesterone, and dyspnea is encountered by 60–70% of normal pregnant women by 30 weeks' gestation [31]. Because dyspnea on exertion is more common especially in the third trimester, diagnosis of respiratory problems may be more difficult than in the non-pregnant state.

The preceding respiratory physiology changes result in a higher PaO_2 (13–14 kPA) and a lower $PaCO_2$ (3.7–4.2 kPA) in the maternal circulation [37]. The higher PaO_2 in the maternal circulation facilitates the transfer of oxygen from the maternal to fetal circulation, whilst the lower $PaCO_2$ in the maternal circulation facilitates transfer of carbon dioxide in the reverse direction.

The lower $PaCO_2$ in the maternal circulation results in a state of respiratory alkalosis. To maintain the maternal pH in the range of 7.40 to 7.45, there is an increase in the excretion of bicarbonate, resulting in lower bicarbonate levels in pregnant women [38]. Lowered bicarbonate levels (18–21 mmol/l) reduce the buffering capacity, making insulin-dependent diabetic pregnant women more susceptible to the complications of diabetic ketoacidosis. The lower bicarbonate levels also shift the maternal oxygen dissociation curve to the right so that the affinity of maternal hemoglobin to oxygen is reduced, facilitating the release of oxygen from maternal hemoglobin for transfer to fetal circulation [39].

During labour and delivery, there is increased hyperventilation. Pain, anxiety and coached breathing during the second stage of labour increase minute ventilation, while narcotics analgesics have the opposite effect. There is therefore a wide variation in minute ventilation and breathing patterns during labour and delivery, with minute ventilation ranging from 7 to 90 litres per minute [40]. Post delivery, lung volume returns to normal, with functional residual capacity and residual volume returning to the baseline within 48 hours [41].

Endocrine changes

During pregnancy, the endocrine system undergoes adaptions to cope with the increased metabolic demands of the mother and fetus. Differentiating endocrine and metabolic disorders from the normal hyper-metabolic state of pregnancy can be challenging.

The hypothalamic pituitary axis is crucial in regulating many key metabolic activities. The levels of many of the hypothalamic releasing hormones increase. Gonadotrophin-releasing hormone (GnRH) and corticotrophin-releasing hormone (CRH) are both expressed by the placenta, and their levels rise during pregnancy. GnRH is needed for the growth and function of the placenta [42]. A rise in CRH may be important to the initiation of both term and preterm labour [43].

The pituitary gland comprising the anterior, intermediate and posterior lobes, increases in size by three-fold. In the anterior lobe, there is hyperplasia and hypertrophy of the lactotrophs during pregnancy. After delivery, the pituitary gland may take up to 6 months to return to its normal size [44]. Gonadotrophin concentrations fall owing to the progressively diminishing response to GnRH, mediated by the increasing oestradiol and progesterone levels during pregnancy [45]. Growth hormone secretion by the pituitary decreases and is replaced by an increase in placenta growth hormone expression [46].

Pregnancy is a state of hypercortisolism. The normal negative feedback loop of a high cortisol level suppressing adrenocorticotrophic hormone (ACTH) release is altered. The placenta secretes both corticotrophin releasing (CRH) and ACTH hormones, leading to high levels of both free and bound cortisol during pregnancy. Serum and urine free cortisol increase three-fold by term. Hepatic synthesis of cortisol binding globulin is also increased. Normal pregnant women however continue to maintain a diurnal variation in ACTH and cortisol levels [47].

Symptoms of Cushing disease (cortisol-excess) characterized by muscle weakness, oedema and weight gain may be difficult to distinguish from the symptoms of normal pregnancy. The glucose intolerance present in Cushing syndrome may be difficult to differentiate from the increasing insulin resistance of a normal pregnancy. The diagnosis of Cushing syndrome during pregnancy becomes more challenging since serum total and free cortisol concentrations and urinary cortisol excretion are already increased in normal pregnant women. Furthermore, in normal pregnancy, cortisol release may not be suppressed with a low dose (1 mg) intravenous dexamethasone [48,49].

The signs and symptoms of adrenal insufficiency (cortisol-deficiency) may be difficult to recognize. Symptoms like vomiting, lethargy, fatigue, low blood pressure and muscle weakness are vague and non-specific. Diagnosis is confirmed by a low cortisol level in the challenge of an ACTH-stimulation test. Yet, the interpretation of cortisol levels from this test can be tricky as levels that may be considered normal in a non-pregnant woman may actually be low in pregnancy [50,51]. In cases of adrenal insufficiency, the stress of labour may culminate in an adrenal crisis resulting in profound hypotensive shock. Treatment with intravenous hydrocortisone should avert an adrenal crisis.

Prolactin secretion from the anterior pituitary increases as pregnancy progresses in preparation for breastfeeding after delivery. Levels of prolactin fall after delivery in non-breastfeeding mothers [52]. The concern is that women with pituitary adenomas may experience worsening of visual fields due to an enlargement in the size of tumor. Microprolactinomas ($<$10 mm) usually cause no problems, as the risk of symptomatic expansion of the tumor is less than 1.5%. Conversely, macroprolactinomas ($>$10 mm) are more problematic causing symptomatic expansion in 4% of treated and 15% of untreated patients. Patients with macroprolactinomas are therefore advised to continue with their medications (dopamine antagonists) during pregnancy [53].

TSH(thyrotropin)-release from the anterior pituitary transiently decreases in the first trimester as a result of the rising human chorionic gonadrotrophin (HCG) [54]. HCG is structurally similar to TSH, and has thyroid-stimulating properties [55]. TSH falls in the first trimester, returning slowly to normal by term. Hyperemesis gravidarum in the first trimester may be associated with a biochemical hyperthyroidism with high levels of free thyroxine and a suppressed TSH, because of HCG's thyrotropic activity. Because estrogen causes a two-fold increase in the synthesis of thyroxine-binding globulin from the liver, circulating levels of total thyroxine (T4) and triiodothyronine (T3) increase. Levels of free-T4 and free-T3 however remain unchanged during pregnancy [54]. Pregnancy is associated with a state of iodine-deficiency because of increased active transport across the feto-placental unit and renal excretion. Despite the increase in production of thyroid hormones, the size of the thyroid gland remains normal, and the presence of any goiter should always be investigated [56]. TSH levels should not be used in isolation for assessing thyroid function because of the variable effects of gestation, and should be interpreted carefully with free-T4 levels [57].

Carbohydrate and fat metabolism undergo changes, such that fatty acids and glycerol are utilized for maternal energy, whilst glucose and amino acids are spared for fetus [58]. Insulin secretion increases due to hyperplasia of beta cells in the pancreas [59]. Fasting glucose drops 10–20% due to increased peripheral glucose utilization [60]. Despite the increase in insulin secretion during pregnancy, there is a relative state of insulin resistance, evidenced by a higher postprandial glucose level [58]. Individuals with marginal pancreatic reserves and obese individuals with pre-existing insulin resistance may not produce enough insulin, thereby leading to gestational diabetes [61]. Because of the increasing insulin resistance with gestation, pregnant women with pre-existing diabetes will require higher doses of insulin as gestation advances [62].

Fat metabolism changes in pregnancy. The second trimester is characterized by increased total cholesterol and triglycerides synthesis and fat accumulation. The third trimester is characterized by maternal consumption of the stored fat [63]. There is also increased lipolysis so that fatty acids and glycerol are released. Glycerol is the preferential substrate for maternal gluconeogenesis, and maternal glucose is the main substrate crossing the placenta for fetal consumption. During maternal fasting, fatty acids can be converted to ketones by the maternal liver to ketones, which can then cross the placenta easily and be utilized by the fetus for oxidative metabolism [63,64] Fat is more than a storage organ, and has endocrine roles. Leptin, an adipocyte-derived hormone, is important in energy hemostasis, and levels are elevated in pregnancies complicated by diabetes or hypertension [65]. Adiponectin, another adipocyte-derived hormone, increases insulin sensitivity, and levels are low in pregnancies complicated by gestational diabetes [66].

The posterior pituitary gland releases oxytocin and antidiuretic hormone (ADH). Clearance of ADH is increased in the placenta, which produces cysteine aminopeptidase with vasopressinase and oxytocinase activity [67]. Although overall ADH levels are unchanged, the increased clearance of ADH may cause some women to develop transient diabetes insipidus during pregnancy [68]. Oxytocin increases continuously across gestation, and is involved in the process of parturition [69]. Nipple stimulation postpartum promotes oxytocin release and milk ejection.

Haematologic changes

Plasma volume increases 30–50%, by 1200–1300 mls in pregnancy. This increase is higher in multigravidas compared to primigravidas. In women with twins, the increase in plasma volume is even greater and can be as high as 70% [70].

Total body water content increases by approximately 6.5 to 8 liters [70]. The increase in oestradiol levels results in the activation of the renin-angiotensin-aldosterone system [71]. This results in increased sodium reabsorption from the kidneys and water retention.

Blood volume starts to increase as early as 7 weeks' gestation by 10–15% and peaks at 30–34 weeks. The 1–2 litres increase in blood volume is important to keep up with the increase in blood flow to organs like uterus and kidneys [72]. The increase in blood volume is also an adaptive mechanism to the inevitable blood loss during delivery of the baby. Because of the significant increase in blood volume during pregnancy, clinical signs of hemorrhage like hypotension and tachycardia may not develop until the pregnant woman has lost at least 30% of her blood volume. Coupled with the difficulty of estimating blood loss at delivery, this means that practicing obstetricians must be vigilant during resuscitation measures to prevent under-replacement of the circulation [22].

There is an increase in red blood cells production, stimulated by an increase in erythropoietin secretion from the kidneys [73]. However, the 18–25% rise in red blood cells is disproportionate to the 30–50% rise in plasma volume, therefore resulting in dilutional anaemia. This is further exacerbated by the transfer of iron stores from mother to fetus [72]. The haemoglobin therefore falls as pregnancy advances, and the anaemia is most noticeable at 30–34 weeks' gestation [72]. The haematocrit falls until the end of second trimester but may stabilise later in pregnancy or even rise near term when the increase in red blood cells becomes proportionate to the increase in plasma volume. However, the haematocrit (32–34%) in a pregnant woman is always lower compared to a non-pregnant woman, and this drop in blood viscosity may be important for increasing blood flow in organs [74]. Maternal iron requirements increase from 5 to 6 mg per day [75]. Overall iron requirements are estimated to be 1000 mg. Anemia resulting from inadequate iron supplementation may result in obstetric complications like preterm delivery and late miscarriages [75].

During pregnancy, there is an adrenocorticoid-mediated leukocytosis resulting in an increase of white cell count. A white cell count of 14,000/mm^3 is normal in pregnancy and may rise even higher to 30,000/mm^3 during labour and the puerperium [76]. The platelet count may be lower in pregnancy because of aggregation, although its value still remains within the normal range [77]. Plasma protein albumin falls, altering peak plasma concentration of drugs that are highly protein-bound [78].

Pregnancy is characterized by a prothrombotic state with a four-fold rise in the risk of venous thromboembolism [79]. Procoagulant factors (factors VII, VIII, IX, X and XII) and fibrinogen increase significantly. In addition, protein-S activity decreases, with an increase in activated protein-C resistance. There is also a decrease in fibrinolysis, mediated by an increase in plasminogen-activator inhibitors 1 and 2 [80]. All these prothrombotic changes, coupled with venous stasis and impaired venous return aggravated by a gravid uterus, make a pregnant woman susceptible to venous thromboembolism, a leading cause of maternal deaths [1,81]. Hence, it is important to screen pregnant women for other venous thromboembolism risk factors and where appropriate, to initiate appropriate prophylaxis e.g., low-molecular-weight heparin or compression stockings [82].

Renal changes

The kidneys are displaced in a cephalad direction by the enlarging uterus. They increase approximately 1 cm in size [83] due to increased vasculature, interstitial volume and dead space [84]. The renal collecting system dilates from the first trimester, a result of a combination of the effects of progesterone, and the compression of the ureters at the pelvic brim [85], resulting in hydroureteronephrosis [86]. Hydroureteronephrosis is more common on the right due to a combination of mechanical compression from the enlarging and dextrorotated uterus and progesterone-mediated smooth muscle relaxation [87]. The physiological dilatation should be taken into account when interpreting radiological studies undertaken for possible urinary tract obstructions. Ureteric compression leads to urine stasis, increasing the incidence of urinary tract infections, nephrolithiasis and pyelonephritis in

pregnancy. At the same time, the bladder loses tone. Therefore, pregnant women complain of increased urinary frequency, urgency and incontinence. These symptoms are compounded in the third trimester as the fetal head engages in the pelvis.

The systemic vasodilatation in pregnancy leads to renal vascular dilatation. Consequently, there is an increase in glomerular filtration rate (GFR) and effective renal plasma flow (RPF) [88]. The glomerular filtration rate (GFR) increases 40–50% by end of the first trimester, peaking at 180 mL/min [89]. This level is maintained until 36 weeks' gestation. The increase in GFR leads to alterations of serum level analytes and may alter clearance of medications that are excreted via the kidneys. Creatinine clearance increases 25% by 4 weeks' gestation, increasing to 45% at 9 weeks' gestation [90]. At the same time, there is increased urinary excretion of protein and albumin mediated by the increase in GFR and changes in charge selectivity of the glomerular membrane. This makes the diagnosis and monitoring of renal diseases during pregnancy complicated. An average of 200 mg to a maximum of 300 mg of protein are excreted daily in a normal pregnancy [91]. Urinary glucose excretion is also increased by increased glomerular filtration and reduced reabsorption in the distal tubules. As such, glycosuria is common in pregnancy and is not a useful finding in the diagnosis of glucose intolerance. Although more sodium is filtered during pregnancy, reabsorption from renal tubules is also increased [92]. There is therefore a net retention of sodium during pregnancy, which helps to sustain the plasma volume increase in the dilated systemic vasculature.

It is important to note that a pregnant woman's physiology does not recognize the renal system as a priority [93]; in situations of haemodynamic compromise such as massive haemorrhage, renal perfusion is preferentially reduced. Consequently, there is a reduction in urine output and increased risk for acute tubular necrosis.

Gastrointestinal changes

As pregnancy gestation advances, the uterus expands and displaces the digestive organs, especially the stomach and intestines. The anatomical alterations can confuse the diagnosis of acute abdominal surgical emergencies. At the same time, the choice and position of surgical incisions can be affected. The peritoneum is stretched which leads to desensitization. Abdominal examination for signs of peritonism can be difficult and potentially inaccurate.

Along with the mechanical effects caused by the enlarging uterus, elevated levels of progesterone contribute to delayed gastric emptying and increased gastrointestinal transit times [94]. Apart from the sensation of bloating and constipation, nausea and vomiting can therefore be common, affecting up to 50% of pregnant women [95]. Gastric acidity is increased because of the increased placental production of gastrin. Together with the reduced oesophageal sphincter tone brought about by increased progesterone, the incidence of reflux oesophagitis and heartburn symptoms is increased, affecting between 50% to 80% of parturients [96].

In labour, anxiety, pain and the use of anticholinergics and opiates further decrease smooth muscle motility [97]. The alterations in gastrointestinal physiology lead to an increased risk of aspiration of gastric contents, especially during administration of general anaesthesia. This risk is further elevated in the obese gravid patient [98]. A pregnant woman planned for general anaesthesia should be fasted 6–8 hours beforehand [98]. To minimize the risks of aspiration, a non-particulate antacid and a H2-receptor antagonist should be prescribed [98]. During intubation, rapid sequence induction and application of cricoid pressure should be practiced. Upon securing the airway, gastric suctioning should be performed.

During pregnancy, serum transaminase and bilirubin levels are decreased slightly whereas serum alkaline phosphatase levels are increased because of placental production.

Summary

Physiological and anatomical adaptations during pregnancy are important for the pregnant woman to cope with the increased metabolic demands crucial for the developing fetus and to survive the demands of childbirth. Understanding these changes is important to recognize pathological deviations in ill obstetric patients and to optimize outcome for both the mother and her baby.

Conflict of Interest

None.

Practice points

- A sound knowledge of physiological and anatomical changes during pregnancy is important to recognize pathological deviations in ill obstetric patients and to optimize care.
- Aortic caval compression from the gravid uterus impedes venous return and reduces maternal cardiac output; maternal resuscitation is more effective if the mother is maintained in a left lateral tilt.
- The significant increase in blood volume during pregnancy means that a pregnant woman has to lose 30% of her circulatory volume before signs of hypovolaemia are apparent. Beware of a rising pulse.
- The increased vascularity and tissue oedema in the upper airway makes intubation during general anaesthesia more difficult. Protecting the airway is important in an unconscious pregnant woman.
- Increased coagulation factors during pregnancy increase the risk of venous thromboembolism, a leading cause of maternal mortality.
- Insulin resistance increases as pregnancy progresses, leading to the manifestation of gestational diabetes in susceptible individuals.
- Gastric emptying is delayed, increasing the risk of aspiration during anaesthesia. Increased gastrointestinal transit time alters pharmacokinetics of drug availabilities.
- The pharmacokinetics of drugs are altered by the alterations in physiology. Medication dosages and regimes may need adjustment.

Research agenda

- Fat is more than a storage organ and has endocrine properties. Obstetric outcomes are worse in obese pregnant individuals. Adipocyte physiology warrants further study in the pathophysiological processes of obstetric illness (e.g. pre-eclampsia).

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