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A DETAILED CLINICAL BIOCHEMISTRY ANALYSIS DURING PREGNANCY: TESTS ASSOCIATED WITH PREGNANCIES AND EARLY CHILD DEVELOPMENT

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ABSTRACT: The physiological and metabolic changes that a pregnant woman must undergo are critical to the success of the pregnancy. Preconception hormonal changes significantly affect the mother's biochemistry in the first trimester of pregnancy. The reproductive hormones, prostaglandins, peptide hormones, and steroids all play a role in the regulation of the mother's capacity to provide nourishment and energy to the developing fetus and placenta. Pregnancy is related with a variety of physiological changes that provide the care, support, and protection of the growing embryo while simultaneously preparing the mother for labor and delivery. These alterations impact the mother's physical, physiological, biochemical, and immunological well-being. Common physiological changes that can occur include motion sickness, irregular menstrual cycles, fluctuations in mood, abdominal swelling, feelings of nausea, fatigue, and sensitivity in the breasts. Additionally, there are immunological and biochemical changes such as alterations in blood levels of specific substances like urea and human chorionic gonadotropin, as well as the presence of immune-modulating agents in the uterus. This overview outlines a detailed clinical biochemistry analysis during pregnancy: tests associated with pregnancies and early child development

Keywords: Biochemistry, Diagnosis, Endocrine, Pregnancy, Screening.

INTRODUCTION

During a typical human pregnancy, which lasts about 280 days, a single diploid cell undergoes development and eventually becomes a newborn weighing around 3.5 kg. The infant is surrounded by roughly 800 ml of amniotic fluid and is supported by a placenta weighing 650 g [1]. The uterus, which initially weighs 40 g before pregnancy, increases in weight to 1.2 kg. In order to sustain the extensive process of growth and development, significant adjustments in the mother's metabolism are necessary to provide nutrients and energy. The pregnant woman experiences a range of physical,

physiological, and biochemical changes during the various trimesters. Some of these changes are transient, while others last for a certain period of time even after the pregnancy ends. Additionally, there are some changes that are permanent [2]. The modifications occurring have an effect on all the organ systems inside the female body. The obvious changes that occur from the time of conception are crucial for providing support and sustenance to both the growing fetus and the mother. In general, the physiological changes that occur during pregnancy may be divided into two categories: local alterations, which specifically affect the reproductive organs, and systemic changes, which impact the whole body. Antenatal care (ANC), sometimes referred to as care throughout pregnancy, is the provision of medical attention by trained healthcare professionals to expectant mothers, with the aim of promoting optimal health for both the mother and the developing baby during the pregnancy. ANC coverage, as defined, refers to the proportion of women aged 15-49 who got antenatal care from a qualified birth attendant (such as a doctor, nurse, or midwife) at least once throughout their pregnancy. Similarly, Focused Antenatal Care (FANC) refers to the proportion of women between the ages of 15 and 49 who have received antenatal care (ANC) on four or more occasions [3]. Countries have evaluated their ANC coverage by means of Demographic and Health Surveys (DHS) in accordance with these criteria. Global statistics indicates that around 86% of pregnant women use antenatal care (ANC) services at least once, although a somewhat lower percentage (62%) have a minimum of four ANC appointments. ANC coverage rates may be obtained via several population-based surveys, such as the Demographic and Health Surveys (DHS), as well as national household surveys in low- and middle-income countries (LMICs). In high-income countries, these rates can be obtained from regular health management information systems and specific perinatal surveys.
The mother's biochemistry is markedly affected by these modifications from the beginning of pregnancy, which start before conception and are managed by a complicated hormonal interaction. Numerous biochemical indicators have a marked shift in normal range as pregnancy goes on as compared to the non-pregnant state. The development of reference intervals especially from a population of healthy pregnant women at distinct gestational stages is necessary for the accurate interpretation of test results for commonly used laboratory procedures. Serious clinical consequences and misunderstandings might result from interpreting test results during pregnancy using reference intervals established on adult, non-pregnant women [4]. This is crucial for the management of women during uncomplicated pregnancies, but it is particularly significant for doctors who are responsible for the treatment of pregnant women with high-risk conditions. This review provides a detailed clinical biochemistry analysis during pregnancy: tests associated with pregnancies and early child development.

HCG levels in normal pregnancy

HCG levels in the blood are modest in normal, non-pregnant persons. Seven days after conception, cultured blastocysts begin to release HCG into the medium [5]. This is also the moment when trophoblasts have HCG messenger RNA. Six to eight days after conception, or around the time of implantation, are the earliest times when HCG may be seen in the mother's blood. Given that the trophoblast has initiated secretion and established direct contact with the mother's circulation, it is probable that the mother's appearance of HCG is a result of both processes. The levels then rise swiftly, with a doubling period of between 1.3 and 1.4 days anticipated. Lenton and colleagues (1991) demonstrated that the exponential increase can be divided into two phases: an initial faster component attributed to the actual implantation process (up to 11 days post-LH surge) and a slower component that occurs when trophoblast HCG and maternal circulating HCG reach equilibrium. Clinical or sub-clinical "biochemical" pregnancies originate from in-vitro fertilization and end in abortion because they produce less HCG [6].

Evaluation of a pregnancy test: Specificity, sensitivity, affordability, and ease of use are the primary factors considered when assessing and contrasting various pregnancy tests. Porter et al. (1988) have provided a comprehensive description of the criteria used to determine specificity. A significant number of samples from both males and non-pregnant women should be used in the testing. At least 50 IU/1 should be the sensitivity [7]. Although there seems to be no justification for their continued use, test kits with sensitivity levels more than 100 IU are nevertheless available. They should never be utilized for particular clinical reasons (such as stomach discomfort), since this might lead to clinically misleading results from a subpar test. Replica determination on samples with HCG levels 50% above and 50% below the limits should be performed to assess the test's precision at the detection limit. Convenience is defined as being straightforward enough for any member of the public to complete the test with ease. Since they are often not educated in lab procedures, the majority of medical professionals may be placed in the same group. The test should be finished in fifteen minutes, including any waiting time for findings that come back later than expected. When considering the value obtained and the demand, these costs are really economical [8]. Doshi (1986) for instance discovered that kits with a reported accuracy of 98–99% could only identify 56% of pregnancies. Although this research dealt with a prior generation of goods, many tests are still evaluated only based on their sensitivity and specificity in the laboratory, extrapolating to their probable performance in the clinic [9].

Biochemical and physiological Changes During Pregnancy

Ø **Biochemical Changes in Pregnancy**

i. Reduction in serum sodium: Serum sodium levels are lowered by three to five milligrams per milliliter as a consequence of increased plasma volume, water, and salt retention. **ii. Reduction in serum creatinine and urea:** The increase in renal blood flow causes a 50% rise in the glomerular filtration rate. Consequently, pregnant women have lower blood concentrations of urea and creatinine than non-pregnant women due to enhanced urea and creatinine clearance [10].

iii. Reduced serum osmolality: Serum osmolality drops during pregnancy as a result of an increase in blood volume. It could be at its lowest point during the first 10 weeks of pregnancy.

iv. Changes in glucose tolerance: The glucose tolerance of an individual changes with each trimester of pregnancy. The relationship between the glucose load or ingestion and the pregnancy's glucose tolerance is direct. The glucose load determines when insulin is secreted, and glucose tolerance is normal in the early stages of pregnancy [11].

v. Changes to fasting blood glucose: The first few months of pregnancy usually cause a 10– 20% drop in fasting blood glucose. To assist the developing fetus, fulfill its energy needs, the first, second, and third trimesters of pregnancy see an increase in the generation of glucose by the liver.

Table 1. Biochemical changes in pregnancy

Parameters	In normal pregnancy	Normal values (pregnancy)
Hemoglobin	Decreased	10.5-13g/dL
WCC (White cell count)	Increased	8-18x109/L
Potassium	Slightly decreased	3.2-4.6mmol/L
Urea	Decreased	1.0-3.8mmol/l
Magnesium	Unchanged	0.6-0.8mmol/l
Fasting glucose	Unchanged	3.0-5.0mmol/l
ALP	Increased	125-250u/l
Serum Calcium	Decreased	2.0-2.4mmol/l
ALT	Unchanged or slightly decreased	1-30 u/l
FT4	Unchanged	10-20 pmol

Ø **Physiological Changes**

- **Endocrine System:** The hypertrophy of prolactin-producing cells causes the pituitary gland to expand during pregnancy. Estrogen and progesterone levels rise, which causes a sharp drop in LH and FSH levels. Prolactin, ACTH, and melanocyte stimulating hormone levels also rise [12]. Similarly, during pregnancy, levels of oxytocin and growth hormone rise while those of ADH remain constant. On the other hand, a drop in osmolality brought on by a low sodium level resets osmo receptors, which in turn promotes thirst and the anti-diuretic hormone (ADH).
- **Adrenal Gland:** The adrenal gland produces glucocorticoids, androgens, and mineralocorticoids. Elevated cortisol, corticosteroid binding globulin, and adrenocorticotropic hormone levels cause symptoms such as high blood pressure, stria, facial plethora, and impaired glucose tolerance [13]. Cortisol is another hormone that elevates blood sugar levels due to its hyperglycemic properties.
- **Haematological Change:** The effects of estrogen and progesterone on the kidneys cause plasma volume to rise by around 45%. These hormones increase the production of rennin, which activates the RAA system and causes salt and water retention. Increased erythropoietin levels increase total red cell mass by 2% until the end of the second trimester, although hemoglobin concentration does not exhibit such dramatic changes since the increase in red cell mass is very minor when compared to plasma volume [14]. This might be referred to as physiological anemia caused by pregnancy. During pregnancy, the platelet count generally decreases. During pregnancy, serum iron levels decrease while total iron binding capacity rises. Clotting factors and fibrinogen rise while fibrinolytic activity decreases, resulting in a hypercoagulable condition [15].
- **Thyroid and parathyroid gland:** High estrogen levels cause a rise in thyroid binding globulin (TBG), which raises T4 and T3 levels throughout the first half of pregnancy. TSH serum concentrations decline throughout the first trimester of pregnancy. Following the first trimester, TSH production is increased. A rise in TSH might be a sign of subclinical hypothyroidism, which is more common in pregnant women, or iodine insufficiency. Consequently, the World Health Organization advises taking 100–200 mg more iodine per day when pregnant. To produce enough thyroid hormones to meet the increased demands of pregnancy, the iodine level should be maintained throughout pregnancy [16]. Since individuals with iodine shortage have a 25% increase in gland size, it is imperative that the gland be frequently examined for the existence of goiter. In a similar vein, a healthy fetus needs a lot of calcium. By the twelveth week of pregnancy, the demand for calcium has doubled. Through modifications in intestinal absorption, parathyroid hormone and calcitonin maintain serum calcium levels in the mother's blood [17].
- **Urinary Tract Changes:** Pregnancy causes a 50-60% rise in glomerular filtration rate (GFR) and renal blood flow due to the increased blood volume and cardiac output. A decrease in blood levels of bicarbonate, uric acid, creatinine, and urea is associated with an increase in GFR [18]. The ureter and renal pelvis smooth muscles are relaxed and enlarged. As the amount of remaining urine increases, the ureters lengthen and bend inward, and the kidneys enlarge. The smooth muscle of the urinary bladder relaxes with an increase in capacity, which raises the risk of urinary tract infections. Acute pyelonephritis, often known as a kidney infection, may affect up to 30 percent of pregnant women [19].

Table 2. Physiological changes during pregnancy.

S. No.	Systems	Changes
1	Cardiovascular system	Tachycardia, high cardiac output, Heart rate
2	Hematological system	Blood cells, clotting factors, Iron deficiency and anemia
3	Respiratory system	Hyper-ventilation, Risk of apnea and dyspnea
4	Gastrointestinal system	Nausea, Vomiting, acidity

Systemic changes and effects on laboratory tests

The interaction of hormonal impacts, variations in blood volume and flow, and changes in metabolism substantially impact the results of several frequently used laboratory tests. It is essential to utilise laboratory reference ranges that are suitable for the specific stage of pregnancy when interpreting test findings [20]. Researchers used a longitudinal study of 29 physically fit pregnant women to create pregnancy reference ranges. The study period included 12 weeks of pregnancy and the 6 weeks after delivery. Ten blood samples were taken during the course of the 34-week period, at predetermined intervals. The results were contrasted with a single blood sample collected from 121 healthy, non-pregnant women of the same age and comparable socioeconomic status [21].

Biochemical assessment of fetal health

The primary objective of foetal evaluation is to guarantee optimal intrauterine growth. Several causes may contribute to foetal growth retardation. The causes of these issues vary, ranging from inadequate maternal nutrition to insufficient functioning of the placenta and foetal abnormalities. Medical imaging is being utilised more and more to identify foetal anomalies, much as how it is used to study the function of the placenta. This reduces the usefulness of biochemical markers [22,23].

Table 3. Biochemical tests for common maternal, placenta and fetal conditions

	Condition	Test
Maternal	Gestational diabetes	Glucose screening tests at 24-28 weeks: 50g challenge test or 2 hour 75g oral glucose tolerance test
	Pre-eclampsia	Urinary position, Renalfunction test, Serum uric acid
Placental	Trophoblastic diseases	HCG, Urinary HCG when indicated
Fetal	Down syndrome	HCG, Maternal serum alpha fetoprotein, pregnancy-associated plasma protein-A, and transnuchal ultrasound between 11 and 13 gestation weeks.
	Neural tube defects	Maternal serum alpha fetoprotein, Amniotic fluid-alpha fetoprotein.

Ø **Role of Motherly Distress in the Developmental Outcomes of Both Fetuses and Children**

Based on the information provided, it can be concluded that maternal distress is a substantial risk factor that may have a notable impact on the psychophysiological development of the foetus. Moreover, prenatal and perinatal risk factors are often linked to it. According to recent research, mothers who experience higher levels of stress, anxiety, and depression throughout their pregnancies are more likely to have preeclampsia, early delivery, low birth weight, and unfavorable outcomes for their unborn child [24, 25].

Moreover, it is crucial to emphasise that maternal anxiety often correlates with distinct alterations in brain structure and anomalies in the operation of the central nervous system. Some changes in brain structure and function make humans more vulnerable during the early stages of development, which in turn affects later stages of development. There are long-term effects on the regulation of neuroendocrine systems and the behavior of the progeny from prenatal stress on the mother, which influences the pregnancy's outcome and causes early programming of the fetal brain's activities [26]. The recorded evidence clearly shows that maternal anxiety during pregnancy has a significant influence on foetal outcomes and the subsequent health outcomes of the child, including cardio-metabolic, pulmonary, atopic, and neurodevelopmentrelated conditions. Maternal distress is known to contribute to several risk factors that can negatively impact various aspects of a child's development [27].

Ø **Cognition**

Cognitive development refers to the intricate mental process that involves the capacity to understand and process information. Maternal prenatal exposure to distress may have an impact on the cognitive development of offspring, leading to inferior mental development. Multiple studies have shown that mothers who experience stressful life events, such as natural catastrophes, and pregnancy anguish have a notably higher likelihood of giving birth to children with inferior cognitive development at various stages of growth [28]. High levels of anxiety throughout the second trimester of pregnancy, as well as both long-term anxiety and short-term anxiety at 32 weeks of gestation, were shown to be associated with worse mental developmental scores in children at 8 and 24 months of age. Higher levels of cortisol in pregnant women throughout the latter stages of pregnancy were linked to decreased brain development in infants at 3 months of age. Contrary to previous research, there is almost no correlation between maternal anxiety during pregnancy and children's general cognitive development at 12 months of age. Researchers looked at how prenatal worry affected children's language development (reading, spelling, writing, and numeracy) [29]. The study's primary objective was to compare how maternal anxiety affected children's expressive and receptive language development. According to study findings, at 30 months of age, children who had mother distress during pregnancy showed worse abilities in both productive and receptive language. The association between 12-month-old infants' language development and worry, stress, and depressive symptoms throughout pregnancy and after delivery [30].

Comprehensive research investigated the influence of prenatal mother anxiety on the cognitive skills of reading and numeracy in children aged 10. In contrast to boys whose mothers experienced maternal distress, this study found no association between prenatal distress and spelling, writing, or numeracy. However, females demonstrated significantly lower levels of success in reading. In contrast to boys in the control group, boys whose mothers had three or more stressful events during pregnancy performed better on writing and numeracy examinations [31, 32].

Ø **Socio-Emotional Development**

Socio-emotional development is a complex process that involves the interaction of maturational and environmental factors. Several studies have shown a link between maternal worry throughout pregnancy and postpartum and a decrease in socio-emotional development [33]. Small research of mother-infant pairs also used diffusion tensor imaging (DTI) to highlight how neonates whose mothers had prenatal depression showed alterations in the neonatal insula, which is associated with internalizing features of behavior [34]. Mother anxiety affects several parts of temperament, according to many research. Regularity, perseverance, and attention span were all negatively impacted in infants (16–18 months) whose mothers had higher stressful life events during the first trimester of pregnancy.

Furthermore, pregnancy-related anxiety was observed to significantly predict fearfulness and falling reactivity in babies at 6 months of age. Infants whose mothers had greater levels of discomfort during the first trimester of pregnancy, such as illness/infection conditions, age, or personal anguish, were shown to be less responsive [35]. Additionally, when a child reaches six months of age, anxiety connected to pregnancy might serve as an indicator of mood disruption. Research has shown that high levels of anxiety during the latter stages of pregnancy may be indicative of a more challenging temperament in newborns. However, anxiety levels throughout pregnancy and anxiety specifically connected to pregnancy do not seem to have a substantial impact on temperament [36-38].

Ø **Fine and Gross Motor Development**

Motor development encompasses the progression of two fundamental components of motor abilities: fine motor skills and gross motor skills. Research examining the motor development of babies at 24-30 months and 36 months of age found that higher levels of anxiety in expectant mothers were linked to lower levels of gross motor development, including delays in both fine and gross motor skills, as well as problem-solving abilities [39,40].

In addition, the evaluation of both fine and gross motor skills was conducted in children at the ages of 2, 6, and 16 months, as well as at 10, 12, and 24 months. At the age of 2 months, there was a positive correlation between the development of both fine and gross motor abilities and the degrees of distress experienced by the mother during and after a traumatic event. Nevertheless, at the age of 6 months, there was a negative correlation between maternal concern and both fine and gross motor abilities. There was no significant link between fine gross motor functioning and maternal distress at 16 months of age. However, there was a negative correlation between gross motor abilities and maternal discomfort. Additionally, when the infants were 10 months old, a negative relationship was seen between the level of anxiety in mothers and their infants' fine motor abilities. However, no significant relationship was identified between maternal anxiety and gross motor skills, visuomotor function, and brain stem function [41]. Furthermore, the motor development of babies who had maternal distress during pregnancy was examined at the ages of 12 and 24 months, as part of their overall development. The findings of this research revealed that babies who were exposed to greater levels of mother anxiety at 12 and 24 months of age had lower scores on the motor scale.
The research investigated the influence of both measurable and perceived stress experienced by pregnant mothers on the physical development of children at the age of 5½ years. The research specifically examined pregnant women who experienced a natural catastrophe. The findings revealed a correlation between prenatal mother stress and the children's ability to coordinate movements on both sides of their body and integrate visual and motor skills. The research investigated the long-term effects of the number and timing of stresses experienced during pregnancy on the physical development of children at ages 10, 14, and 17 [42].

Ø **Neurodevelopmental Disorders**

The two most prevalent neurodevelopmental disorders are attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). These disorders are characterized by anomalies in development that affect social, intellectual, personal, or occupational functioning. The association between a mother's anxiety before to and during delivery and her chance of developing ASD and ADHD has been the subject of several studies. Based on these research, there is evidence that stress during pregnancy is linked to a higher chance of ASD or ADHD diagnoses in children after the age of three [43]. The timing of stress exposure during pregnancy for both ASD (in the first and third trimester) and ADHD (in the third trimester) was shown to be significantly correlated with gender differences in ADHD diagnoses. At the age of 6 years and 6 months, both boys and girls, regardless of gender, scored higher on autism-like traits in several studies looking at the symptoms of Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) in children whose mothers experienced prenatal distress. These scores were especially high when mothers experienced multiple stressful events during pregnancy [44]. But according to a study looking at the spectrum of symptoms associated with autism in kids who have already received an ASD diagnosis and were distressed during womb development, the severity of autism symptoms is only higher in kids whose moms went through a lot of stressful situations when they were pregnant. Language (syntax, semantics, coherence, and stereotyped language), communication, and behavior (repetitive and restricted behavior) all shown a considerable increase in symptoms. According to the research, prenatal stress may be able to change an autism spectrum disorder’s trait [45].

Complications of pregnancy

Most pregnancy tests are conducted primarily to satiate the curiosity of the lady and her family members. Additionally, there are significant medical reasons. These conditions include instances when the lady need to contemplate modifying her way of life to mitigate potential hazards to the foetus. Illustrative instances comprise smoking, substance abuse, and excessive alcohol use. Furthermore, pregnancy may need special medical intervention, particularly in cases when the mother has diabetes or heart problems. Furthermore, it has been advised that all women who are getting endometrial biopsy during the late luteal phase of their menstrual cycle should also receive a pregnancy test [46]. A crucial medical reason is to examine women with stomach symptoms that may or may not be linked to a pregnancy. Ninety-five percent or more of women with ectopic pregnancy get a positive pregnancy test (> 25 IU/1). Although falsenegative findings are rare, when an assay with a sensitivity of 200 IU/1 is used, the rate rises to 11.9%. Although the historical evidence seems to clearly rule out pregnancy, research suggests that around 10% of women may still be pregnant. Research conducted on female accident victims found that 2% of them were pregnant, as determined by random pregnancy tests. If the test yields a negative result, it may be confidently inferred that pregnancy is not present in the case. Conversely, if the test shows a positive result, it is advisable to do a laparoscopy to definitively determine the presence or absence of an ectopic pregnancy. Implementing this approach has significantly enhanced the precision of diagnosing ectopic pregnancy, resulting in a notable decrease in needless laparoscopies and other specialised examinations. The diagnostic method has been facilitated by the extensive accessibility of uncomplicated and highly responsive testing [47].

Nutrition in pregnancy and programming of offspring health

The development of an embryo and foetus at each stage is reliant on and affected by the right supply of nutrients from the mother. The timing of dietary deficiencies seems to have varying effects on the development of adult disorders by influencing the postnatal physiological processes. The notion of initiating programming for lifetime health at an early stage has been well established [48]. Research suggests that when pregnant women experience nutrient restriction during the first trimester, it may lead to a higher likelihood of developing coronary heart disease, elevated lipids, and obesity. Nutrient restriction in the middle of pregnancy is associated with kidney diseases, while restriction during late gestation is linked to reduced glucose tolerance in adulthood [49]. Furthermore, there is a growing body of evidence indicating that nutrition during early life can have a long-lasting impact on overall health, including the risk of developing infections, allergies, autoimmune diseases (, bone health, neural and brain function, and obesity. While it is evident from animal research that alterations in macro- or micronutrient consumption may have substantial impacts on foetal growth and development, the degree to which these results apply to humans remains uncertain. During pregnancy, the body undergoes metabolic and physiological changes to ensure that the foetus receives the necessary nutrients [50]. During the first three months of pregnancy, there is a notable accumulation of fat in the adipose tissue, leading to an overall rise in the mother's body weight. This might result in sufficient availability of maternal lipids not only during the latter stages of pregnancy, but also during breastfeeding, when the heightened breakdown of fats raises the levels of circulating lipids to support the development of the newborn.

Conclusion

Pregnancy is marked by a variety of physiological, biochemical, and physical changes that occur during the three trimesters. It is essential to be aware of the many changes that occur throughout a regular pregnancy in order to take proper measures or actions as soon as possible if there are any deviations from the usual changes, in order to prevent the pregnancy being lost. Biochemical signs are critical in assessing the health of pregnant women, placentas, and fetuses. Ultrasonography continues to be essential for the detection and support of a diverse array of associated disorders, despite the growing quality and prevalence of the technology. Further investigation into development is necessary, along with a thorough evaluation of the readiness and support provided to women.

Refrences

1. Nanda S, editor. Evaluation and Management of High-Risk Pregnancies: Emerging Research and Opportunities: Emerging Research and Opportunities.
2. Forestier F, Daffos F, Rainaut M, Bruneau M, Trivin F. Blood chemistry of normal human fetuses at midtrimester of pregnancy. Pediatric research. 1987 Jun;21(6):579-83.

3. Goodlin RC. History of fetal monitoring. American Journal of Obstetrics and Gynecology. 1979 Feb 1;133(3):323-52.
4. Goodlin RC. History of fetal monitoring. American Journal of Obstetrics and Gynecology. 1979 Feb 1;133(3):323-52.
5. Kalashilpa CH. Study on relationship between thyroid hormones and glucose homeostasis among post menopausal diabetic women (Doctoral dissertation, BLDE (Deemed to Be University)).
6. Binny RN, Lustig A, Hendy SC, Maclaren OJ, Ridings KM, Vattiato G, Plank MJ. Realtime estimation of the effective reproduction number of SARS-CoV-2 in Aotearoa New Zealand. PeerJ. 2022 Oct 17;10:e14119.
7. Land KJ, Boeras DI, Chen XS, Ramsay AR, Peeling RW. REASSURED diagnostics to inform disease control strategies, strengthen health systems and improve patient outcomes. Nature microbiology. 2019 Jan;4(1):46-54.
8. Yuksel M, Luo W, McCloy B, Mills J, Kayaharman M, Yeow JT. A precise and rapid early pregnancy test: Development of a novel and fully automated electrochemical point-of-care biosensor for human urine samples. Talanta. 2023 Mar 1;254:124156.
9. Fagnant DJ, Kockelman KM. The travel and environmental implications of shared autonomous vehicles, using agent-based model scenarios. Transportation Research Part C: Emerging Technologies. 2014 Mar 1;40:1-3.
10. Bawah AT, Kuffour FA, Boateng MA, Seini MM, Amoah P, Ussher FA, Alidu H. Effect of pregnancy on the metabolism of creatinine, urea and uric acid among pregnant women at the volta regional hospital.
11. Edelson PK, James KE, Leong A, Arenas J, Cayford M, Callahan MJ, Bernstein SN, Tangren JS, Hivert MF, Higgins JM, Nathan DM. Longitudinal changes in the relationship between hemoglobin A1c and glucose tolerance across pregnancy and postpartum. The Journal of Clinical Endocrinology & Metabolism. 2020 May;105(5):e1999-2007.
12. Reis FM, D'Antona D, Petraglia F. Predictive value of hormone measurements in maternal and fetal complications of pregnancy. Endocrine reviews. 2002 Apr 1;23(2):230-57.
13. Auchus RJ, Parker KL, Rainey WE. The adrenal glands. Textbook of endocrine physiology. Sixth ed. New York, NY: Oxford University Press, USA. 2012:346-80.
14. Stachenfeld NS, Taylor HS. Progesterone increases plasma volume independent of estradiol. Journal of applied physiology. 2005 Jun;98(6):1991-7.
15. Fisher AL, Nemeth E. Iron homeostasis during pregnancy. The American journal of clinical nutrition. 2017 Dec 1;106:1567S-74S.
16. Moleti M, Trimarchi F, Vermiglio F. Thyroid physiology in pregnancy. Endocrine Practice. 2014 Jun 1;20(6):589-96.
17. Zimmermann MB, Boelaert K. Iodine deficiency and thyroid disorders. The lancet Diabetes & endocrinology. 2015 Apr 1;3(4):286-95.
18. Beers K, Patel N. Kidney physiology in pregnancy. Advances in Chronic Kidney Disease. 2020 Nov 1;27(6):449-54.
19. Hill WG. Control of urinary drainage and voiding. Clinical Journal of the American Society of Nephrology. 2015 Mar 1;10(3):480-92.
20. Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. Obstetrics & Gynecology. 2009 Dec 1;114(6):1326-31.
21. Klajnbard A, Szecsi PB, Colov NP, Andersen MR, Jørgensen M, Bjørngaard B, Barfoed A, Haahr K, Stender S. Laboratory reference intervals during pregnancy, delivery and the early postpartum period. Clinical chemistry and laboratory medicine. 2010 Feb 1;48(2):237-48.
22. Tran HA. Biochemical tests in pregnancy. Australian prescriber. 2005 Aug 1;28(4).
23. Teasdale S, Morton A. Changes in biochemical tests in pregnancy and their clinical significance. Obstetric medicine. 2018 Dec;11(4):160-70.
24. Goldenberg RL, Goepfert AR, Ramsey PS. Biochemical markers for the prediction of preterm birth. American journal of obstetrics and gynecology. 2005 May 1;192(5):S36-46.

25. Nava S, Bocconi L, Zuliani G, Kustermann A, Nicolini U. Aspects of fetal physiology from 18 to 37 weeks' gestation as assessed by blood sampling. Obstetrics & Gynecology. 1996 Jun 1;87(6):975-80.
26. Hershman JM. Physiological and pathological aspects of the effect of human chorionic gonadotropin on the thyroid. Best Pract Res Clin Endocrinol Metab 2004;18:249-65.
27. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139:137-47.
28. Gelman R, Lucariello J. Role of learning in cognitive development. Stevens' handbook of experimental psychology: Learning, motivation, and emotion. 2002;3:395-443.
29. Hobel CJ. Intrapartum clinical assessment of fetal distress. American Journal of Obstetrics and Gynecology. 1971 Jun 1;110(3):336-42.
30. Stiles J, Brown TT, Haist F, Jernigan TL. Brain and cognitive development. Handbook of child psychology and developmental science. 2015 Feb 24:1-54.
31. Li J, Robinson M, Malacova E, Jacoby P, Foster J, Van Eekelen A. Maternal life stress events in pregnancy link to children's school achievement at age 10 years. The Journal of pediatrics. 2013 Mar 1;162(3):483-9.
32. Khajeei D, Neufeld H, Donelle L, Meyer SB, Neiterman E, Ike NA, Li JZ. Maternal health literacy and health numeracy conceptualizations in public health: A scoping review. Health & Social Care in the Community. 2022 Nov;30(6):e3534-46.
33. Goldschmidt TJ. The exploration of preschool teachers' understanding and classroom experience of socio-emotional development in early childhood and the role it plays in school readiness.
34. Sacchi C, De Carli P, Mento G, Farroni T, Visentin S, Simonelli A. Socio-emotional and cognitive development in intrauterine growth restricted (IUGR) and typical development infants: early interactive patterns and underlying neural correlates. rationale and methods of the study. Frontiers in Behavioral Neuroscience. 2018 Dec 18;12:315.
35. Lentoor AG. The relationship between psychosocial factors and poor neurocognitive and socio-emotional development in children perinatally infected with HIV in South Africa (Doctoral dissertation).
36. Sacchi C. Child development following fetal adversities. From neural to interactive processes of socio-emotional vulnerability in Intrauterine Growth Restricted infants.
37. Kim KK, Fang W, Liu AY, Panesar D, Xiao NG. Altered development of face recognition among infants born amid the COVID-19 pandemic. Journal of Experimental Child Psychology. 2024 Aug 1;244:105942.
38. Beckwith L, Rozga A, Sigman M. Maternal sensitivity and attachment in atypical groups. Advances in child development and behavior. 2003 Jan 1;30:231-74.
39. Gallahue DL, Ozmun JC. Motor development in young children. InHandbook of research on the education of young children 2014 Jan 27 (pp. 123-138). Routledge.
40. Gallahue DL. Understanding motor development in children and youth. InProceedings of The 6th international scientific and expert symposium "Contemporary views on the Motor Development of a Child 2010 (pp. 17-23).
41. Goodway JD, Ozmun JC, Gallahue DL. Motor development in young children. InHandbook of research on the education of young children 2013 Jan 17 (pp. 103-115). Routledge.
42. Cao X, Laplante DP, Brunet A, Ciampi A, King S. Prenatal maternal stress affects motor function in 5½-year-old children: Project Ice Storm. Developmental psychobiology. 2014 Jan;56(1):117-25.
43. Ronald A, Pennell CE, Whitehouse AJ. Prenatal maternal stress associated with ADHD and autistic traits in early childhood. Frontiers in psychology. 2011 Jan 19;1:223.
44. Bendiksen B, Aase H, Diep LM, Svensson E, Friis S, Zeiner P. The associations between pre- and postnatal maternal symptoms of distress and preschooler's symptoms of ADHD, oppositional

defiant disorder, conduct disorder, and anxiety. Journal of Attention Disorders. 2020 May;24(7):1057-69.

45. Oerlemans AM, Burmanje MJ, Franke B, Buitelaar JK, Hartman CA, Rommelse NN. Identifying unique versus shared pre-and perinatal risk factors for ASD and ADHD using a simplex-multiplex stratification. Journal of abnormal child psychology. 2016 Jul;44:92335.
46. Lindhard A, Ravn V, Bentin-Ley U, Horn T, Bangsboell S, Rex S, Toft B, Soerensen S. Ultrasound characteristics and histological dating of the endometrium in a natural cycle in infertile women compared with fertile controls. Fertility and sterility. 2006 Nov 1;86(5):1344-55.
47. Redelmeier DA, May SC, Thiruchelvam D, Barrett JF. Pregnancy and the risk of a traffic crash. Cmaj. 2014 Jul 8;186(10):742-50.
48. Guilloteau P, Zabielski R, Hammon HM, Metges CC. Adverse effects of nutritional programming during prenatal and early postnatal life, some aspects of regulation and potential prevention and treatments. J Physiol Pharmacol. 2009 Oct 1;60(Suppl 3):17-35.
49. Langley-Evans SC. Nutrition in early life and the programming of adult disease: a review. Journal of Human Nutrition and Dietetics. 2015 Jan;28:1-4.
50. Sullivan EL, Nousen EK, Chamlou KA. Maternal high fat diet consumption during the perinatal period programs offspring behavior. Physiology & behavior. 2014 Jan 17;123:236-42.