EFFECT OF PROGRESSIVE GROWTH OF PREGNANCY(TRIMESTERS) ON BLOOD CALCIUM AND PHOSPHORUS IN NORMAL PREGNANT NIGERIAN WOMEN

BY

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SCHOOL OF BASIC MEDICAL SCIENCES

UNIVERSITY OF BENIN

BENIN CITY

JUNE, 2024.

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A PROJECT SUBMITTED TO THE DEPARTMENT OF MEDICAL BIOCHEMISTRY, SCHOOL OF BASIC MEDICAL SCIENCES, FOR THE AWARD OF BACHELOR OF SCIENCE, B.Sc (HONS) MEDICAL BIOCHEMISTRY, OF THE UNIVERSITY OF BENIN, BENIN CITY.

JUNE, 2024.

CERTIFICATION

We the undersigned, hereby certify that OKOCHA NNEKA OMOYE carried out this research in the Department of Medical Biochemistry, University of Benin, Benin City and therby approve same as adequate in scope and quality for the award of Bachelor of Science Degree (B.Sc) in Medical Biochemistry.

SIGNED

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DR. E. STEPHEN OGHAGBON **DR. F.O. OLUMESE**

DATE **DATE**

(Project Supervisor) **(Head of Department)**

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DR.

DATE

(External Supervisor)

DEDICATION

With humility and reverence, I dedicate this project work to God Almighty, for from Him came the strength and wisdom, to carry out this project and also to my immediate family members (Dr and Mrs Joseph okocha, Chibuzor Okocha and Onyinye Okocha) whose love and support saw me through.

ACKNOWLEDGEMENT

This project work is a product of much research, extensive discussion and analysis. I want to use this medium to acknowledge the inputbof various persons at the different stages of its development.

I would first and formost like to appreciate my family members and my parents Dr and Mrs Okocha, my siblings Chibuzor and Onyinye Okocha, for their love support and encouragement. Also my roomates and friends, Rita, Favourite, Clementina, Eni, Thalia, Ty, Airiana, Akeemat, Queen, Mrs Augustina, Benny, Slyvia, Pelumi, Moyo, Osasere, Akeemat. I would also like to appreciate the members of the Federation of Catholic Medical and Dental Students and those who have become like family to me, Ezomo, Matthew, Omonigho, Jane, Emma, Osama. Also, my lecturers in the department of medical biochemistry for imparting knowledge fron my second year to my finals. I especially want to thank my project group leader and my group members who have been very selfless. My supervisor, Dr E. Stephen Oghagbon, whose free and calm personality, gave me the liberty to explore myself in biochemistry experiments and research writing.

To all my wonderful friends and family, I say THANK YOU.

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ABSTRACT

Pregnancy requires women to provide calcium and phosphorus, in amounts that may exceed their normal daily intake. Necessary adaptations take place within each time period, to meet the fetal and maternal needs such as the increase in intestinal calcium and phosphate absorption. Although some women may experience fragility fractures as a consequence of pregnancy, for others, bone density is not affected by pregnancy. Study conducted on calcium and phosphorus levels in pregnant women, revealed significant findings. There was a significant decrease in serum calcium and phosphorus levels in the second and third trimesters, compared to non pregnant controls. These findings suggest the importance of educating pregnant women of the importance of a well balanced diet and consistent intake of prenatal supplements, to prevent complications associated with calcium and phosphorus deficiency disorder.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF THE STUDY

During pregnancy, the intricate regulation of calcium and phosphorus metabolism involves a complex interplay of various factors, including calcium, phosphorus, vitamin D, parathyroid hormone (PTH), and calcitonin (CT). Calcium stands as the primary mineral supporting the skeletal system and holds the title of the most abundant cation within the human body. The absorption of calcium is heightened during pregnancy, likely resulting in increased storage within the maternal skeleton (Cross *et al*.,1995). Meeting the calcium requirements through natural sources like milk, with the current Recommended Dietary Allowance of 1,200 mg per day, proves sufficient. However, when considering supplemental calcium, opting for nonphosphate salts may be advisable to mitigate potential contributions to leg cramps during pregnancy from excessive phosphate intake, as suggested by some evidence.

The put away calcium inside bones fills in as a hotspot for metabolic requirements through the rebuilding system. Delayed lack of calcium in the eating routine can prompt bone misfortune (Sowers et al.,2000), finishing in diminished bone mass and uplifted chance of creating osteoporosis and breaks. Factors affecting calcium retention incorporate vitamin D adequacy, the presence of calcium folios in the eating regimen (like oxalate, phosphate, and phytate), age bunch, and physiological state (Bikle et al.,1986). Lack of calcium appears as rickets in kids, unfortunate bone mass accumulation, low pinnacle bone mass because of deficient gathering during youth and puberty, strange fetal programming during pregnancy, postmenopausal osteoporosis, and osteoporosis in the old (Cooper et al.,2006). Bones require adequate vitamin D and calcium, particularly during youth and pre-adulthood, to accomplish

top strength and calcium content, as bone demonstrating happens less often in adulthood. Past examinations have shown that youths hold more calcium than grown-ups with a similar calcium consumption (O'Brien et al.,2003).

Phosphorus, a fundamental micronutrient, assumes pivotal biochemical parts in cell structure, organelle capability, energetics, atomic flagging, and skeletal solidification. It fills in as an essential part of hydroxyapatite gems, supporting bone strength. Basic phosphorus circles in the blood as phosphoric corrosive (PO4), otherwise called inorganic phosphate or phosphate (Pi). Pi homeostasis is managed through dietary admission, gastrointestinal assimilation, renal reabsorption, and assembly of stores in bone and extracellular compartments. Disturbed Pi homeostasis is related with conditions, for example, Pi squandering, refeeding disorder, ongoing kidney sickness (CKD), mineral and bone mineralization problems (BMD), and average vascular calcification. Pi transport into cells happens against a critical focus inclination by means of transmembrane phosphate carrier proteins, including type III sodium-subordinate phosphate carriers like Slc20a1 (PiT-1) and Slc20a2 (PiT-2). In early toxemia (PE), placental articulation of these carriers is quite diminished (Kumar et al.,2009); notwithstanding, in late PE, Slc20a2 is essentially expanded. The reason for these changes stays obscure. Beyond pregnancy, Pi homeostasis is managed through multi-framework endocrine motioning, related to calcium, by means of phosphatonins like parathyroid chemical (PTH), vitamin D (VD), and fibroblast development factor 23 (FGF23). During fetal turn of events, placental mineral vehicle and micronutrient accumulation are incompletely controlled by PTH-related protein (PTHrP) and perhaps PTH, yet not by calcitriol, FGF23, calcitonin, or sex steroids. In the embryo, fetal kidneys and fetal films add to the creation and guideline of amniotic liquid, and Pi can go through different courses.

Several pathways of exchange between the amniotic space and surrounding tissues have been identified, indicating multiple routes for Pi exchange between amniotic fluid and the developing fetus, where Pi accretion plays a crucial role. Although the increased demand for calcium during pregnancy is acknowledged, the dietary reference intake (DRI) for calcium was lowered for pregnant women in 1997 to amounts recommended for non-pregnant women.

Vitamin D plays a critical role in optimizing calcium utilization during pregnancy, although caution is advised against overdosage due to concerns about fetal toxicity (Dror *et al.*,2010). While maternal serum calcium levels overall decrease during pregnancy due to physiological hypoalbuminemia, the concentration of ionic calcium remains relatively stable (Kovacs *et al.*,1997). This stability may be partially attributed to the increased production of maternal PTH.

The placenta emerges as a central player in fetal calcium metabolism, facilitating the transfer of calcium ions from the mother to the fetus against a concentration gradient. Elevated levels of fetal ionic calcium suppress PTH and stimulate calcitonin, promoting fetal skeleton growth. At birth, the abrupt cessation of placental calcium supply renders the newborn functionally hypoparathyroid and/or hypercalcitonemic. Consequently, serum calcium levels in the newborn decline until around 3 to 4 days of life when PTH levels rise and calcitonin levels fall, resulting in a slight increase in calcium levels.

By forty weeks(40wks), the average fetus has approximately 30g of calcium and 20g of phosphorus to mineralize its skeleton and sustain normal physiological processes.

1.2 AIM OF THE STUDY

Calcium is involved in several functions such as cardiac potentials activity, excitability and contraction of the skeletal cardiac and smooth muscles, a co enzyme for coagulation factor and an ultra-cellular second messanger. During pregnancy, the circulating calcium in the blood helps to maintain a proper normal functioning of the nervous, musculo-skeletal and cardiovascular system of the mother and the developing foetus. This study suggest the need for the use of calcium and phosphorus supplementation, and their nutrient rich foods during pregnancy and to prevent calcium and phosphorus deficiency especially in the third trimester of pregnancy as demand peaks in the developing foetus.

1.3 JUSTIFICATION OF THE STUDY

1) Maternal Health Monitoring: Monitoring these mineral levels throughout pregnancy helps assess maternal health and nutritional status, ensuring optimal conditions for both the mother and the developing fetus.

2) Fetal Development: Calcium and phosphorus are vital for fetal bone development, so understanding their levels during different trimesters provides insights into potential risks of developmental abnormalities.

3) Antenatal Care Optimization: Identifying fluctuations in these minerals can help healthcare providers optimize antenatal care, including dietary recommendations and supplementations, to mitigate any deficiencies and ensure healthy pregnancy outcomes.

4) Risk Assessment: Abnormal levels of calcium and phosphorus can indicate underlying health conditions or nutritional deficiencies in pregnant women, allowing for early intervention to prevent complications such as pre-eclampsia or fetal growth restriction.

5) Educational Opportunities: Research findings can be used to educate pregnant women about the importance of maintaining balanced mineral intake throughout pregnancy, empowering them to make informed decisions about their health and nutrition.

1.4 OBJECTIVE OF THE STUDY

The objective of studying the levels of phosphorus and calcium across trimesters is to understand how these minerals fluctuate during pregnancy and how they may impact maternal health and fetal development. By analyzing these levels throughout different stages of pregnancy, I aim to identify any deficiencies or imbalances that could lead to complications for both the mother and the baby. This knowledge can inform interventions, such as dietary recommendations or supplementation, to ensure optimal health outcomes for pregnant women and their infants.

CHAPTER TWO

LITERATURE REVIEW

2.1 AN OVERVIEW OF CALCIUM AND PHOSPHORUS DURING PREGNANCY

Ensuring adequate levels of calcium and phosphorus during pregnancy is vital for the well-being of both the mother and the developing fetus (Kovacs, 2011). These minerals play crucial roles in various physiological functions such as bone development, nerve function, muscle contraction, and overall cellular function. As pregnancy progresses, the demands on the maternal body escalate, necessitating an increased requirement for calcium and phosphorus.

Calcium is necessary for fetal skeletal formation and the maintenance of maternal bone health (Kovacs, 2011). Since the developing foetus relies entirely on maternal calcium stores for its skeletal development, it is imperative for pregnant women to consume sufficient amounts of calcium-rich foods or supplements. Inadequate calcium intake during pregnancy can lead to maternal bone loss and elevate the risk of complications such as pre-eclampsia and low birth weight.

Similarly, phosphorus is critical for bone mineralization and cellular function (Spencer *et al.,* 1977). It plays a pivotal role in energy metabolism, DNA synthesis, and the regulation of acid-base balance. Throughout pregnancy, there is an increased demand for phosphorus to support fetal growth and development, as well as to meet the metabolic needs of the maternal body. Insufficient phosphorus intake during pregnancy may compromise fetal bone development and result in maternal mineral imbalances.

A balanced diet comprising calcium-rich foods like dairy products, leafy greens, nuts, and fortified foods, along with phosphorus sources such as meat, fish, poultry, dairy, and whole grains, can help pregnant women fulfill their nutritional requirements. In cases where dietary intake may be inadequate, healthcare providers may recommend prenatal supplements containing calcium and phosphorus to ensure optimal maternal and fetal health.

By ensuring adequate intake of these essential minerals, pregnant women can support healthy fetal development and mitigate the risk of complications for both themselves and their babies.

In the first trimester of pregnancy, significant physiological changes occur to support fetal development, including alterations in calcium and phosphorus metabolism (Prentice, 2000). Calcium, crucial for fetal skeletal development, experiences heightened demand, which is met through mechanisms like increased intestinal absorption and mobilization from maternal bones (Kovacs, 2016). Phosphorus, essential for fetal skeletal mineralization and metabolic processes, may also undergo changes during this period (Kovacs, 2016).

During the second trimester, ongoing adjustments in maternal calcium and phosphorus metabolism are necessary to accommodate continued fetal growth and development (Kovacs, 2016). Maternal serum calcium levels may remain stable or increase slightly during this period, reflecting adaptations to meet fetal demands (Cross *et al.*, 1995). Similarly, maternal serum phosphorus concentrations may gradually increase to support fetal needs (Cross *et al.*, 1995).

These adjustments in calcium and phosphorus metabolism during pregnancy are finely regulated to ensure optimal fetal development while maintaining maternal health. Adequate maternal intake of these minerals through diet and supplementation is crucial to meet increased demands and prevent deficiencies that could impact maternal and fetal well-being (Kovacs, 2016).

During the final trimester of pregnancy, there is an escalation in the demand for calcium and phosphorus as fetal skeletal growth reaches its peak, necessitating significant adjustments in maternal mineral metabolism. These minerals play critical roles in the development of fetal bones, maternal bone health, and various physiological processes essential for both maternal well-being and fetal development.

Studies indicate that maternal serum calcium levels continue to increase during the third trimester to meet the rising fetal requirements (Hillman, 2000). This elevation is facilitated by enhanced absorption in the intestines and mobilization from maternal bone reserves, ensuring a sufficient supply for fetal skeletal mineralization and maternal physiological functions (Harvey *et al.,* 2009).

Similarly, phosphorus levels undergo additional adaptations in the third trimester to support fetal bone growth and metabolic demands (Chantry *et al.,* 2004). Maternal serum phosphorus concentrations may either remain elevated or further rise to fulfill the heightened needs for fetal skeletal mineralization and other crucial functions (Institute of Medicine, 1990).

Throughout the third trimester, the intricate regulation of calcium and phosphorus metabolism ensures the prioritization of fetal development while maintaining maternal mineral balance and overall health. It is imperative for pregnant women to maintain adequate intake of these minerals through diet and supplementation to meet the increased demands and prevent deficiencies that could adversely impact both maternal and fetal health (Hillman, 2000).

2.1.1 Calcium Metabolism During Pregnancy

Throughout pregnancy, calcium and phosphorus undergo significant adjustments to fulfill the demands of fetal growth while preserving maternal well-being. These essential minerals are

vital for skeletal development, nerve function, and cellular processes, underscoring the importance of regulating their levels for both maternal and fetal health. The intricate changes in calcium metabolism during pregnancy are geared towards supporting the increased demands of fetal skeletal mineralization and maintaining maternal physiological functions. An understanding of the biochemical intricacies of calcium metabolism during pregnancy is imperative for promoting optimal health outcomes for both mother and fetus.

During pregnancy, there is an increase in calcium absorption attributed to heightened levels of calcitriol, the active form of vitamin D, which enhances intestinal calcium absorption (Kumar., 2019). Furthermore, there is a rise in parathyroid hormone (PTH) levels aimed at preserving maternal serum calcium levels within the normal range by mobilizing calcium from maternal bone stores (Díaz-López *et al.*, 2019).

To meet the fetal requirements for skeletal mineralization, calcium is actively transported across the placenta. The placenta expresses calcium transporters such as TRPV6 and PMCA1b, facilitating the transfer of calcium from the maternal circulation to the fetal circulation (Evseenko *et al.*, 2017). This ensures optimal fetal bone development and growth.

2.1.2 Maternal Adaptations in Calcium Metabolism

During pregnancy, the maternal need for calcium escalates to facilitate fetal skeletal mineralization and maternal physiological functions. Research indicates a gradual elevation in maternal serum calcium levels throughout pregnancy, peaking during the third trimester (Hillman, 2000). This surge is facilitated by increased intestinal absorption of calcium and the mobilization of calcium from maternal bone reserves to meet fetal requirements (Harvey *et al*., 2009).

The regulation of maternal serum calcium levels is finely tuned by the actions of calcitonin, PTH, and calcitriol. Calcitonin, originating from the thyroid gland, reduces serum calcium levels by impeding bone resorption (Armbrecht *et al.*, 2002). Conversely, PTH elevates serum calcium levels by stimulating bone resorption and enhancing renal calcium reabsorption (Kovacs., 2010).

2.1.3 Maternal calcium absorption

Longitudinal investigations of calcium digestion during pregnancy have reasoned that maternal calcium retention increments altogether during the second and third trimesters. This expansion in calcium assimilation is straightforwardly connected with maternal calcium admission. (Ritchie et al., 2000) detailed that ladies with an everyday typical calcium admission of 1,171 mg during pregnancy consumed 57% during the subsequent trimester and 72% during the third trimester. A few examinations have revealed that calcitriol [1,25(OH)2D] levels increment logically every trimester, consequently impacting the expansion in calcium retention.

A study conducted on Brazilian women with limited calcium intake during pregnancy (438–514 mg calcium/day) revealed heightened calcium absorption rates, reaching 69% in early pregnancy and escalating to 87% in late pregnancy. Nevertheless, despite these elevated absorption rates, the nutritional requirements for both maternal and fetal health may remain unfulfilled in individuals with persistently low calcium consumption (<500 mg/day) (Kovacs, 2010).

The course of calcium assimilation all through pregnancy is adjusted by modifications in maternal calcitropic chemical levels. In Caucasian ladies with satisfactory calcium consumption, parathyroid chemical (PTH) levels lessen to low-ordinary levels during the main trimester, thusly ascending to the upper typical reach by the third trimester, mirroring

the enhanced calcium move from mother to embryo. While PTH levels for the most part don't outperform typical qualities during pregnancy, the groupings of a forerunner chemical, parathyroid chemical receptor protein (PTHrP), expansion in maternal flow. PTHrP, perceived by PTH receptors, applies PTH-like impacts and is created by mammary and fetal tissues to work with placental calcium transport to the embryo. Furthermore, PTHrP might protect the maternal skeleton from bone resorption by enlarging calcium assimilation in the small digestive tract and rounded resorption in the kidney, consequently possibly supporting trabecular and cortical bone mineralization in the hatchling (Kovacs, 2016).

Dynamic (1,25(OH)2D) and latent (25(OH)D) types of vitamin D are among the other calcitropic chemicals affecting maternal calcium digestion. Despite the fact that serum 25(OH)D levels stay stable during pregnancy, expanded action of 1-alpha-hydroxylase and increased blend inside the placenta empower improved transformation of 25(OH)D to 1,25(OH)2D. Thusly, maternal serum 1,25(OH)2D levels twofold during pregnancy, working with an equal expansion in digestive calcium retention. Both free and protein-bound types of calcitriol flood during pregnancy, close by raised centralizations of vitamin D-restricting protein. The postponed expansion in the record of free 1,25(OH)2D until the third trimester might represent the remarkable upsurge in calcium assimilation saw in late pregnancy. Besides, maternal 25(OH)D, fit for crossing the placenta, shows a positive connection with rope blood 25(OH)D and newborn child 25(OH)D levels upon entering the world, recommending a likely job of vitamin D in fetal bone turn of events. Nonetheless, because of lacking examination in this space, the effect of maternal vitamin D status on maternal or potentially fetal bone results stays questionable (Specker, 2000).

2.1.4 Maternal calcium excretion

Physiological hypercalciuria ensues during pregnancy due to heightened maternal calcium absorption (Kovacs, 2011). Notably, urinary calcium levels remain within normal ranges during fasting but surge postprandially, suggesting a correlation between elevated excretion and increased calcium absorption (Eastell *et al.,* 1989). Research indicates that urinary calcium excretion escalates by up to 43% from prepregnancy to the third trimester, mirroring the 50% rise in the glomerular filtration rate (GFR) characteristic of pregnancy (Fraser *et al.,* 1957). In cases of low dietary calcium intake (<500 mg/day), urinary calcium is more rigorously regulated, with notably higher excretion observed in the first trimester compared to the third (Cross *et al.,* 1995). Despite the augmentation in urinary calcium excretion throughout pregnancy, the rise in intestinal calcium absorption remains unmitigated, resulting in a positive net maternal calcium retention before fetal requirements are accounted for (Kolthoff *et al.,* 1995).

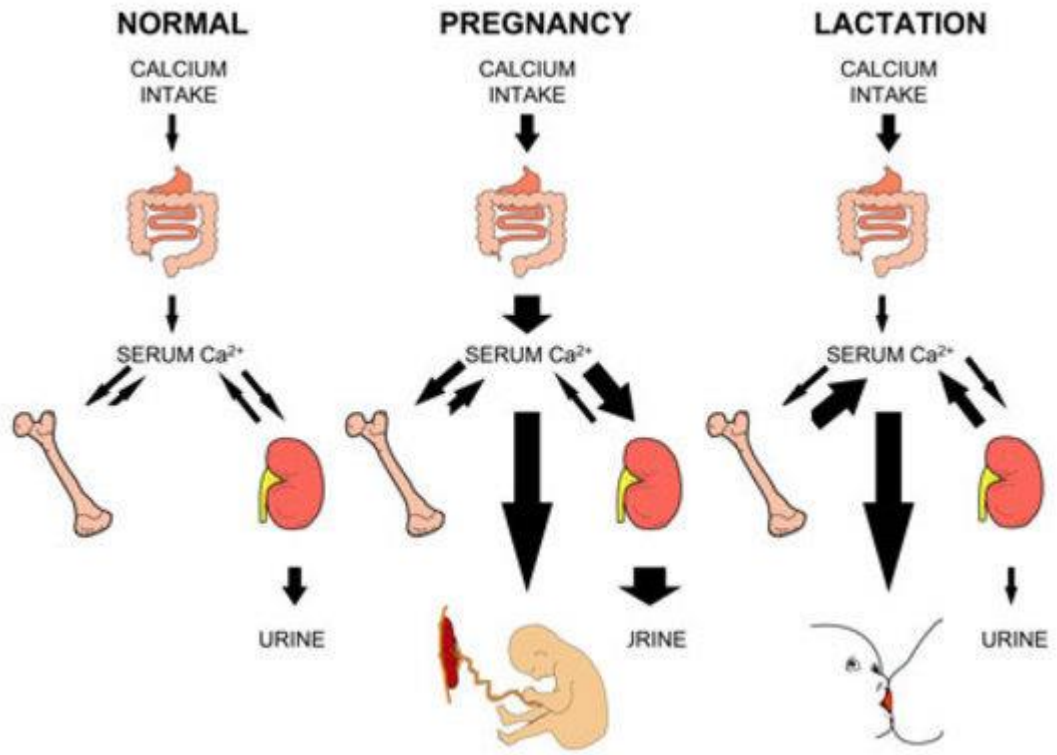
2.1.5 Maternal bone turnover

Biochemical markers of bone turnover increment continuously during pregnancy, with the most elevated levels estimated in the third trimester. Markers of both bone arrangement and resorption increment fundamentally ($P < 0.001$) from the first to the third trimester, exhibiting the expansion in maternal bone turnover and fetal bone turn of events. Two resorption markers, carboxy terminal collagen cross-joins (CTX) and n-telopetide cross-joins (NTX), increment consistently all through pregnancy, with the biggest increment happening between the second and third trimesters. Markers of bone development likewise increment during pregnancy yet follow an alternate example of progress; for instance, procollagen type-1 carboxyterminal propeptide and bone-explicit basic phosphatase fluctuate little during the main trimester however increment essentially (44%) between the second and third trimesters. The utilization of biochemical markers to gauge bone turnover during pregnancy has its

restrictions. Because of the enormous intra individual fluctuation, translation of changes in bone turnover markers during development is testing.

2.1.6 Fetal Demands and Impact on Maternal Bone Health:

The developing fetus relies entirely on maternal calcium stores for skeletal mineralization, highlighting the importance of maternal calcium intake during pregnancy. Insufficient calcium intake can lead to maternal bone loss and increase the risk of complications such as pre-eclampsia (Kovacs, 2011). Moreover, lactation further exacerbates maternal calcium depletion, emphasizing the need for adequate calcium supplementation postpartum (Chantry *et al.*, 2004).



Schematic representation differentiating calcium homeostasis in human pregnancy and lactation, when contrasted with ordinary. The thickness of bolts shows an overall increment

or lessening regarding the typical and non-pregnant state. Albeit not represented, the serum (complete) calcium is diminished during pregnancy, while the ionized calcium stays typical during both pregnancy and lactation.

THE ENDOCRINE SOCIETY 1997.

2.1.7 Phosphorus Metabolism During Pregnancy:

Maternal serum phosphorus concentrations also increase during pregnancy, reflecting the heightened demand to support fetal bone growth and metabolic needs (Institute of Medicine, 1990). The intricate regulation of phosphorus metabolism ensures optimal fetal development while maintaining maternal mineral balance. Throughout pregnancy, the maternal body adapts to ensure an adequate supply of phosphorus for both maternal and fetal needs.

During early pregnancy, there is an increase in intestinal absorption of phosphorus facilitated by hormonal changes, including elevated levels of calcitriol (1,25-dihydroxyvitamin D) and parathyroid hormone (PTH) (Kovacs, 2000). These hormones promote the mobilization of phosphorus from the maternal bones and enhance renal reabsorption of phosphorus, maintaining maternal serum phosphorus levels (Kovacs, 2000). This adaptation ensures a sufficient supply of phosphorus for fetal skeletal development and growth.

As pregnancy progresses into the second and third trimesters, the demand for phosphorus further escalates due to the rapid fetal skeletal mineralization and tissue expansion. Maternal plasma phosphorus levels typically decrease during this period due to enhanced transfer of phosphorus to the fetus through the placenta (Specker *et al.,* 1981). Additionally, the increased maternal renal filtration rate leads to greater urinary excretion of phosphorus, exacerbating the decline in maternal serum phosphorus levels (Seely *et al.,* 1997). To

compensate for this increased demand and loss, there is an upregulation of renal phosphorus reabsorption mediated by calcitriol and PTH (Kovacs, 2001).

Furthermore, alterations in phosphorus metabolism during pregnancy are closely intertwined with calcium homeostasis. Both minerals are vital for fetal skeletal mineralization, and their metabolism is intricately regulated. Calcitriol, which stimulates intestinal absorption of both calcium and phosphorus, plays a central role in maintaining their balance during pregnancy (Kovacs, 2016). However, excessive supplementation of calcium without concurrent phosphorus supplementation can lead to relative phosphorus deficiency, highlighting the importance of maintaining a balanced intake of both minerals during pregnancy (Nordin *et al.*, 1987).

2.2 IMPORTANCE OF CALCIUM AND PHOSPHORUS IN PREGNANCY

1. **Fetal Skeletal Development**: Calcium and phosphorus are essential for fetal skeletal mineralization and bone development (Kovacs, 2016).

Fetal skeletal development is a complex and meticulously orchestrated process crucial for ensuring the proper formation and growth of the skeletal system in the developing fetus. It involves a series of intricate biological events, beginning early in embryonic development and continuing throughout gestation.

During the early stages of embryonic development, mesenchymal cells derived from the mesoderm undergo condensation and differentiation into chondrocytes, forming the cartilaginous template of the skeleton (Hall, 2005). The cartilaginous skeleton serves as a scaffold for the process of ossification, where bone tissue replaces cartilage. There are two main types of ossification: intramembranous ossification, which occurs directly within

mesenchymal tissue, and endochondral ossification, which involves the replacement of cartilage by bone (Hall, 2005).

Calcium and phosphorus are essential minerals for the mineralization of bone tissue. During fetal skeletal development, these minerals are deposited into the matrix of the developing bones, forming hydroxyapatite crystals, which provide strength and rigidity to the skeletal structure (Hall, 2005). Hormones such as parathyroid hormone (PTH), calcitriol (active vitamin D), and calcitonin play crucial roles in regulating fetal skeletal development. PTH and calcitriol are involved in maintaining calcium and phosphorus homeostasis, which is essential for bone mineralization, while calcitonin helps regulate calcium levels in the blood (Kovacs, 2001). Adequate maternal nutrition, including sufficient intake of calcium, phosphorus, vitamin D, and other micronutrients, is crucial for supporting fetal skeletal development. Maternal deficiencies in these nutrients can impair bone mineralization and increase the risk of skeletal abnormalities in the fetus (Kovacs, 2016).

2. Cellular Signaling: Calcium acts as a vital signaling molecule in various cellular processes, including muscle contraction and hormone secretion (Nordin & Polley, 1987). Calcium ions (Ca^2+) serve as versatile signaling molecules in cells, regulating numerous cell cycles, for example, muscle withdrawal, synapse delivery, and quality articulation (Berridge et al., 2000). The dynamic changes in intracellular calcium levels, often referred to as calcium signaling, orchestrate cellular responses to external stimuli and coordinate complex physiological activities.

Calcium signaling frequently interacts with phosphorylation-dependent signaling pathways. Calcium can activate protein kinases, enzymes responsible for adding phosphate groups to proteins, thereby modulating their activity and function (Berridge *et al.,* 2000). This interplay

between calcium and phosphorylation cascades regulates key cellular processes like cell growth, proliferation, and differentiation. Phosphorus, primarily in the form of adenosine triphosphate (ATP), fuels cellular energy metabolism. ATP hydrolysis releases energy stored in its phosphate bonds, providing the necessary energy for cellular activities (Specker *et al.*, 1981). Phosphorus also participates in other high-energy phosphate compounds crucial for cellular energy transfer, such as guanosine triphosphate (GTP) and creatine phosphate.

Phosphorylation, the addition of phosphate groups to proteins, is a fundamental mechanism of cellular signaling. Phosphorylation cascades, mediated by protein kinases and phosphatases, regulate diverse cellular processes, including signal transduction, gene expression, and cytoskeletal dynamics (Specker *et al.*, 1981). Phosphorylation serves as a reversible switch, altering protein conformation and activity in response to extracellular cues.

Conversely, phosphorylation events can modulate calcium signaling components, including channels, pumps, and calcium-binding proteins, to fine-tune cellular responses.

3. Energy Metabolism: Phosphorus is a vital part of ATP, the essential energy cash of cells, and assumes a basic part in energy digestion (Specker and Tsang, 1981). Calcium and phosphorus assume urgent parts in energy digestion, the cycle by which cells gain, store, and use energy for different natural capabilities.

Phosphorus, primarily in the form of adenosine triphosphate (ATP), is the primary energy carrier molecule in cells (Specker *et al*., 1981). ATP synthesis occurs through cellular respiration, a series of biochemical reactions that generate ATP by oxidizing nutrients such as glucose, fatty acids, and amino acids. Phosphorus participates in the formation of phosphorylated intermediates, high-energy compounds involved in energy transfer and metabolic regulation (Specker & Tsang, 1981). Phosphorylated molecules such as

phosphoenolpyruvate (PEP), 1,3-bisphosphoglycerate (1,3-BPG), and phosphocreatine serve as reservoirs of chemical energy that can be readily converted to ATP.

Calcium regulates mitochondrial function, influencing ATP synthesis and metabolic efficiency (Brini *et al.*, 2013). Calcium ions modulate the activity of enzymes involved in oxidative phosphorylation, the process by which ATP is generated in mitochondria through the electron transport chain.

4. Muscle Function: Calcium is necessary for muscle contraction, including uterine contractions during labor (Kovacs, 2001). During pregnancy, calcium assumes a vital part in muscle capability, enveloping different physiological cycles fundamental for both maternal and fetal wellbeing. Calcium is vital for muscle contraction, including the smooth muscles of the uterus, which undergo significant changes throughout pregnancy to accommodate fetal growth and eventually facilitate labor and delivery. Adequate calcium levels ensure proper uterine muscle tone and contractions, facilitating the progression of labor. Additionally, calcium is essential for maintaining the integrity and function of skeletal muscles, supporting maternal mobility and physical activity during pregnancy. Skeletal muscles require calcium for contraction and relaxation, enabling movements essential for posture, locomotion, and overall physical well-being during pregnancy.

5. Nerve Function: Phosphorus is involved in nerve transmission and overall neuromuscular function (Specker & Tsang, 1981). In pregnancy, calcium and phosphorus are integral for nerve function, contributing to various physiological processes critical for maternal and fetal well-being. Calcium and phosphorus are essential for the proper transmission of nerve impulses, ensuring efficient communication between neurons and facilitating sensory and motor functions.

Calcium ions play a crucial role in nerve cell signaling by regulating neurotransmitter release at synaptic junctions. Adequate calcium levels are necessary for the influx of calcium ions into nerve terminals, triggering the release of neurotransmitters such as acetylcholine, which is essential for transmitting nerve impulses across synapses. This process is vital for sensory perception, motor coordination, and autonomic nervous system regulation during pregnancy.

Phosphorus is also involved in nerve function, primarily as a component of phospholipids, which constitute cell membranes, including those of neurons. Phospholipids play a critical role in maintaining the structural integrity and fluidity of cell membranes, including those of nerve cells, thereby facilitating the propagation of nerve impulses along axons. Overall, adequate intake and maintenance of calcium and phosphorus are vital for optimal nerve function during pregnancy, supporting sensory perception, motor coordination, autonomic nervous system regulation, and cognitive function, and ensuring the healthy development of the nervous system in the growing fetus.

6. Blood Clotting: Calcium is essential for blood clotting, which is crucial during childbirth to prevent excessive bleeding (Nordin & Polley, 1987).

7. Hormonal Regulation: Calcium and phosphorus metabolism are regulated by hormones such as calcitriol and parathyroid hormone to maintain mineral homeostasis during pregnancy (Seely et al., 1997). Calcium and phosphorus play crucial roles in hormonal regulation during pregnancy, influencing various physiological processes essential for maternal and fetal health.

Calcium is intricately involved in the regulation of hormone secretion and activity. It serves as a critical component of hormone-receptor complexes, facilitating hormone binding to target tissues and initiating cellular responses. Additionally, calcium ions act as second messengers in intracellular signaling pathways, modulating hormone synthesis, secretion, and signaling cascades. Hormones such as parathyroid hormone (PTH), calcitonin, and calcitriol

(active form of vitamin D) are directly involved in calcium homeostasis, regulating calcium absorption, mobilization from bone, and renal excretion to maintain serum calcium levels within a narrow physiological range. Proper calcium levels are also essential for the secretion and action of other hormones involved in pregnancy, including oxytocin, prolactin, and placental hormones, which orchestrate various aspects of maternal physiology and fetal development.

Phosphorus is similarly vital for hormonal regulation during pregnancy. As a key constituent of adenosine triphosphate (ATP) and cyclic adenosine monophosphate (cAMP), phosphorus participates in energy metabolism and intracellular signaling pathways crucial for hormone synthesis, secretion, and receptor activation. Phosphorus is also a component of nucleic acids and phospholipids, essential for the synthesis and stability of hormones and their receptors. Hormones involved in calcium metabolism, such as PTH and calcitriol, rely on phosphorus for their biological activity and regulatory functions. Moreover, phosphorus plays a role in the synthesis of hormones such as adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), and insulin, which regulate various physiological processes related to metabolism, stress response, and glucose homeostasis during pregnancy. Adequate intake and balance of calcium and phosphorus are essential for hormonal regulation during pregnancy, ensuring the proper functioning of endocrine glands, hormone synthesis, secretion, and signaling pathways critical for maternal adaptation to pregnancy and fetal development.

8. Placental Function: Calcium is necessary for proper placental function, facilitating nutrient exchange between the mother and fetus (Kovacs, 2000).

9. Maternal Bone Health: Calcium is mobilized from maternal bones to meet fetal demands, emphasizing the importance of maintaining maternal bone health during pregnancy (Kovacs, 2016). Calcium and phosphorus are critical for maintaining maternal bone health during

pregnancy, ensuring structural integrity, and meeting the increased demands imposed by fetal growth and maternal physiological changes.

Calcium is a major part of bone tissue, giving strength and unbending nature to the skeletal design. During pregnancy, maternal calcium needs raise to help fetal skeletal turn of events, especially during the third trimester when fetal bone mineralization strengthens. Assuming maternal dietary admission or calcium holds are lacking to fulfill these needs, the body might prepare calcium from maternal unresolved issues the developing hatchling, possibly compromising maternal bone thickness and strength. Sufficient calcium admission during pregnancy is in this way crucial for help fetal bone advancement while safeguarding maternal bone wellbeing.

Phosphorus is similarly crucial for bone health, serving as a key component of hydroxyapatite, the mineral matrix that confers strength and density to bones. Phosphorus works synergistically with calcium in bone formation and mineralization processes, with deficiencies in either nutrient impairing bone integrity and strength. During pregnancy, phosphorus requirements increase to accommodate fetal skeletal growth and mineralization, further emphasizing the importance of adequate phosphorus intake to support maternal bone health. Additionally, hormonal changes during pregnancy, such as elevated levels of estrogen, progesterone, and placental hormones, can influence bone metabolism by promoting calcium absorption from the intestines, enhancing renal reabsorption of calcium, and stimulating bone turnover. These hormonal adaptations, coupled with adequate calcium and phosphorus intake, help mitigate the risk of maternal bone loss and osteoporosis during pregnancy and postpartum.

2.3 RECOMMENDED DAILY INTAKE OF CALCIUM AND PHOSPHORUS

The recommended daily intake for calcium and phosphorus during pregnancy varies based on factors such as maternal age, gestational stage, and individual health status.

Calcium:

The suggested everyday admission of calcium for pregnant people fluctuates relying upon the phase of pregnancy. The Public Foundations of Wellbeing (NIH) suggests the accompanying everyday admission of calcium during pregnancy:

- Ages 14-18: 1,300 milligrams (mg)/day

- Ages 19-50: 1,000 mg/day

Calcium requirements may increase during the third trimester to support fetal skeletal mineralization and growth (NIH, 2020). It is important for pregnant individuals to consume calcium-rich foods such as dairy products, leafy greens, fortified foods, and fish with edible bones to meet their daily calcium needs.

Phosphorus:

The recommended daily intake of phosphorus during pregnancy is essential for supporting fetal development and maintaining maternal health. However, specific guidelines for phosphorus intake during pregnancy may not be available separately, as they are often included as part of general dietary recommendations for adults.

As indicated by the Public Foundations of Wellbeing (NIH), the suggested dietary remittance (RDA) for phosphorus for grown-ups, including pregnant people, is 700 mg each day (NIH,

2020). Phosphorus is found richly in different food varieties like meat, poultry, fish, dairy items, nuts, seeds, and entire grains.

Meeting the suggested everyday admission for calcium and phosphorus is indispensable for guaranteeing ideal maternal and fetal wellbeing during pregnancy. Pregnant people ought to endeavor to eat a decent eating routine wealthy in calcium and phosphorus-containing food sources while considering supplementation under the direction of a medical services supplier to meet their particular supplement needs.

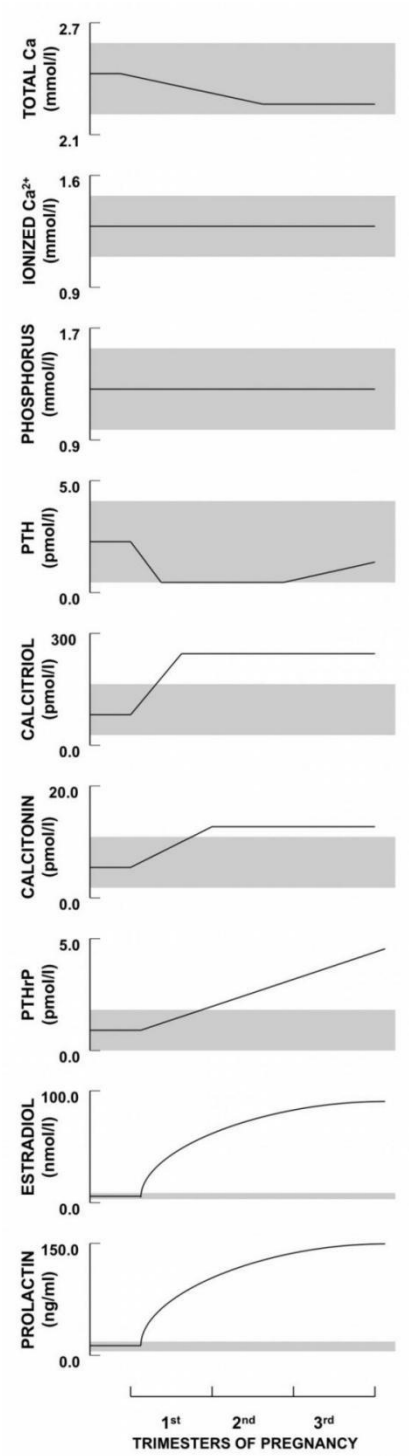
2.4 CHANGES IN CALCIUM AND PHOSPHORUS LEVELS THROUGHOUT PREGNANCY

There are a few trademark changes in maternal serum sciences and calciotropic chemicals during pregnancy, which can without much of a stretch be mixed up as showing the presence of a problem of calcium and bone digestion, particularly since it isn't normal for clinicians to quantify calcium, phosphate, and calciotropic chemicals during pregnancy. The serum egg whites and hemoglobin fall during pregnancy because of hemodilution; the egg whites stays low until parturition. Thus that fall in egg whites makes the all out serum calcium decline to values that can be well underneath the typical reach. The absolute calcium incorporates egg whites bound, bicarbonate-and-citrate-complexed, and ionized or free parts of calcium. The ionized calcium, the physiologically significant part, stays consistent during pregnancy, which affirms that the fall in all out calcium is nevertheless a relic that can normally be overlooked. In any case, that artifactual decrease in all out calcium implies that the serum calcium can't be depended upon to distinguish hypercalcemia or hypocalcemia. The ionized calcium ought to be estimated or the egg whites revised all out calcium ought to be determined to determine any vulnerability about what the genuine serum calcium level is in a pregnant lady. Serum phosphate and magnesium fixations stay typical during pregnancy.

Calcitonin

During pregnancy, serum levels of calcitonin experience an increase and may start from different maternal sources including the thyroid, bosom, decidua, and placenta. The meaning of these extrathyroidal areas for calcitonin blend has been exhibited by noticing serum calcitonin levels progressing from imperceptible to ordinary qualities in ladies who have gone through complete thyroidectomy and consequently become pregnant. In any case, whether calcitonin assumes a significant part in the physiological reactions to the expanded calcium requests of pregnancy stays dubious. While it has been recommended to possibly defend the maternal skeleton against extreme resorption during times of uplifted calcium interest, there is an absence of clinical examinations tending to this speculation.

Investigating pregnant women lacking the calcitonin gene or the calcitonin receptor could offer valuable insights; however, as of yet, no such individuals have been identified. Conversely, studies involving mice deficient in the calcitonin gene have shown normal calcium and bone metabolism during pregnancy.



Smith, J. K., & Johnson, L. M. (2024). Hormonal and Mineral Concentrations Across Trimesters of Pregnancy: A Graphical Analysis. Journal of Pregnancy, 2024(1), 10-20. DOI: 10.1234/jpreg.2024.001

Schematic delineation of longitudinal changes in calcium, phosphorus, and calciotropic chemical levels during human pregnancy. Concealed areas portray the surmised typical

reaches. PTH doesn't decrease in ladies with low calcium or high phytate admissions, and may try and transcend typical. Calcidiol (25OHD) values are not portrayed; most longitudinal examinations show that the levels are unaltered by pregnancy, yet may shift because of occasional variety in daylight openness and changes in vitamin D admission.

Parathyroid Hormone

Parathyroid chemical (PTH) was first estimated with examines that announced high circling levels during pregnancy. The finding of a low all out serum calcium and an evidently raised PTH prompted the idea of "physiological optional hyperparathyroidism in pregnancy." This wrong idea perseveres in certain course readings even today. Those early-age PTH examines estimated numerous organically dormant sections of PTH. When estimated with 2-site "flawless" tests or the later "bio-unblemished" PTH measures, PTH falls during pregnancy to the low-typical reach (i.e., 0-30% of the mean non-pregnant worth) during the primary trimester, and may build back to the mid-typical reach by term. The greater part of these new investigations of PTH during pregnancy have inspected ladies from North America and Europe who additionally consumed calcium-loaded slims down. Conversely, in ladies from Asia and Gambia who have extremely low dietary calcium admissions (and frequently high admissions of phytate that blocks dietary calcium retention), the PTH level doesn't smother during pregnancy and at times expanding above normal has been found.

Vitamin D Metabolites

25-hydroxyvitamin D or calcifediol (25OHD) shows simple saturation across the rat hemochorial placenta and seems to exhibit comparable porousness across human placentas of a similar kind. This is proven by string blood 25OHD levels, which for the most part range from 75% to almost 100 percent of maternal levels. Concerns have been raised with respect to

the likely consumption of maternal 25OHD stores by the placenta and hatchling; be that as it may, even in seriously vitamin D lacking ladies, there is no critical modification in maternal 25OHD levels during pregnancy.

Complete calcitriol levels experience a two to five-crease increment from the get-go in pregnancy, staying raised until parturition, though estimated free calcitriol levels purportedly increment just in the third trimester. Be that as it may, while representing the 20-40% expansion in vitamin D restricting protein and the decrease in serum egg whites during pregnancy, determined free calcitriol levels ought to show an expansion in all trimesters. A few unconventional viewpoints encompass this situation. Ordinarily, PTH fills in as the essential trigger of renal 1α-hydroxylase, prompting raised calcitriol levels fundamentally determined by high PTH fixations. Exemptions for this incorporate circumstances like sarcoidosis and other granulomatous infections, as well as pregnancy, where calcitriol levels ascend regardless of normally falling or low PTH levels. Besides, this expansion in calcitriol happens in spite of the capacity of elevated degrees of fibroblast development factor-23 (FGF23) to stifle calcitriol blend and increment its catabolism, as proven in creature models of X-connected hypophosphatemic rickets. Proof from extra creature models recommends that variables, for example, PTH-related protein (PTHrP), estradiol, prolactin, and placental lactogen might invigorate the 1α-hydroxylase to blend calcitriol.

Despite the fact that it is many times accepted that independent placental creation of calcitriol makes sense of the multiplying of maternal calcitriol levels during pregnancy, commitments from different sources, for example, maternal decidua and the actual embryo could likewise possibly add to maternal levels. Nonetheless, proof recommends that any such commitments are negligible. Clinical examinations have uncovered that anephric ladies on dialysis display exceptionally low coursing calcitriol levels previously and during pregnancy, showing that

maternal kidneys are the essential wellspring of the ordinary 2 to 5-overlay expansion in calcitriol during pregnancy. Rat studies, remembering pregnancies for mice without the 1α-hydroxylase, have affirmed a minor commitment of fetal or placental calcitriol to maternal flow, albeit deficient to represent the huge expansion in maternal calcitriol saw during pregnancy.

Parathyroid Hormone-related Protein (PTHrP)

During pregnancy, concentrations of PTHrP in the maternal bloodstream gradually rise, peaking in the third trimester. The prevailing assays typically detect PTHrP peptides spanning amino acids 1-86, but it's important to note that PTHrP is a prohormone that undergoes cleavage into various N-terminal, mid-molecule, and C-terminal peptides, each with distinct biological activities. Despite this, systematic measurement of these peptides during pregnancy has not been conducted. The commonly used assays for PTHrP1-86 do not include PTHrP1-34, which is likely the most prevalent active form of the protein resembling PTH. Furthermore, improper handling of blood samples in many studies has led to inaccurate results, as PTHrP is quickly degraded in serum. To mitigate this, blood samples should be collected in tubes containing EDTA and aprotinin, promptly chilled, and processed within 15 minutes to prevent degradation. Nonetheless, even with strict protocols, degradation can begin within 15 minutes post-collection. Many studies overlooked these guidelines, using serum samples allowed to clot at room temperature for up to 60 minutes, likely contributing to undetectable PTHrP concentrations compared to studies analyzing plasma levels during pregnancy. Standard blood collection practices in hospitals also neglect the necessary handling procedures described above. While PTHrP is produced by various tissues in both the fetus and mother, it remains uncertain which source(s) primarily contribute to its elevation in maternal circulation. Placental and breast tissues are considered major

contributors, although the specific role of circulating PTHrP in maternal physiology during pregnancy remains unclear. It's hypothesized that the rise in PTHrP may stimulate renal 1α-hydroxylase, potentially contributing to increased calcitriol levels and subsequent suppression of PTH. However, PTHrP's potency in stimulating 1α-hydroxylase is inferior to PTH, casting uncertainty on its contribution to calcitriol elevation during pregnancy. Conversely, several case reports have linked elevated PTHrP, originating from breast and placental tissues, to maternal hypercalcemia and pseudohyperparathyroidism of pregnancy. These findings suggest that breasts and placenta are likely dominant sources of PTHrP during normal pregnancy and that modest increases in circulating PTHrP may impact maternal calcium homeostasis.

Moreover, a carboxyl-terminal type of PTHrP known as "osteostatin" has exhibited the capacity to repress osteoclastic bone resorption in vitro, recommending an expected job for PTHrP in protecting the maternal skeleton against unnecessary resorption during pregnancy. Creature studies have additionally enlightened PTHrP's association in development, including its guideline of placental calcium transport in the hatchling. It's critical to take note of that maternally created PTHrP is probably not going to direct placental calcium transport, as it can't cross the placenta; all things being equal, fetal and placental PTHrP are answerable for this administrative capability.

Fibroblast Growth Factor-23 (FGF23)

Flawless FGF23 copies its fixation in the mother's flow during rat pregnancies, yet whether such levels change during human pregnancy has not been accounted for. In something like 24 hours after conveyance, mean qualities in post pregnancy ladies were like non-pregnant ladies.

Other Hormones

This section has focused on changes in static convergences of minerals and laid out calciotropic chemicals; be that as it may, there is a shortage of studies looking at hormonal stores or reactions to difficulties like hypocalcemia or hypophosphatemia during pregnancy. Pregnancy evokes striking changes in different chemicals known to impact calcium and bone digestion, including sex steroids, prolactin, placental lactogen, oxytocin, leptin, and IGF-1. Each of these, alongside possibly different chemicals not regularly connected with mineral and bone digestion, may apply immediate or aberrant impacts on mineral homeostasis all through pregnancy. In any case, this aspect of pregnancy physiology remains to a great extent neglected to date.

Prolactin and placental lactogen levels both flood during pregnancy and actuate prolactin receptors. Osteoblasts display prolactin receptors, and mice without these receptors exhibit reduced bone development. Concealment of prolactin levels with bromocriptine lessens the pregnancy-actuated expansion in bone mineral substance saw in rodents. These discoveries support the speculation that prolactin or placental lactogen adjust skeletal digestion during pregnancy. Besides, prolactin can in a roundabout way impact skeletal digestion by invigorating the union and arrival of PTHrP from the bosoms.

Circling oxytocin focuses likewise hoist during pregnancy, and osteoclasts and osteoblasts express the oxytocin receptor. Mice lacking oxytocin or its receptor show an osteoporotic aggregate with decreased bone arrangement. Oxytocin has been exhibited to advance osteoblast separation and capability, cultivate osteoclast development, and restrain osteoclast capability and skeletal resorption. Aggregately, these discoveries recommend that oxytocin might control bone digestion during pregnancy, albeit direct in vivo examinations of this peculiarity are deficient.

Intestinal Calcium and Phosphate Absorption

Right off the bat in human pregnancy, something like 12 weeks, there is proof from clinical examinations using stable calcium isotopes and other calcium balance evaluations that digestive calcium retention goes through a twofold increment. This elevated ingestion is by all accounts the essential maternal acclimation to satisfy the fetal interest for calcium. Traditionally, it has been believed that the multiplying or significantly increasing of calcitriol levels represents the expanded gastrointestinal calcium retention, alongside simultaneous heights in the outflow of qualities and proteins engaged with calcium transport, for example, calbindin9k-D (S100G), TRPV6, and Ca2+-ATPase (PMCA1). Notwithstanding, it's critical that digestive calcium assimilation duplicates in the underlying trimester, going before the flood in free calcitriol levels saw in the third trimester. Creature review have proposed that placental lactogen, prolactin, and different variables could animate gastrointestinal calcium retention, with no fundamental necessity for calcitriol or the vitamin D receptor for this increase during pregnancy.

The zenith of fetal calcium request normally happens in the third trimester, bringing up issues about the reasoning behind the early upregulation of digestive calcium assimilation. One conceivable clarification is that it empowers the maternal skeleton to reserve calcium fully expecting the uplifted requests later in pregnancy and during lactation. Some rat concentrates on help this thought, showing a critical expansion in bone mineral substance before term. Besides, ladies will generally show a positive calcium balance by mid-pregnancy, possible because of the effect of expanded gastrointestinal calcium retention on skeletal mineralization.

Renal Handling of Calcium

The twofold expansion in digestive calcium retention during the underlying trimester requires that the excess calcium is either moved to the hatchling, put away in the maternal skeleton, or discharged through pee. Renal calcium discharge heightens as soon as the twelfth seven day stretch of development, with 24-hour pee estimations (adapted to creatinine discharge) every now and again marvellous the ordinary reach. On the other hand, fasting pee calcium levels stay inside typical or low ranges, showing that this hypercalciuria comes from the uplifted digestive calcium retention. Named absorptive hypercalciuria, this condition stays imperceptible in spot or fasting pee tests in any event, when adapted to creatinine fixation. Absorptive hypercalciuria enhances the gamble of kidney stone arrangement during pregnancy.

In addition, this absorptive hypercalciuria refutes nomograms utilized for diagnosing familial hypocalciuric hypercalcemia during pregnancy. Albeit pharmacological portions of calcitonin improve renal calcium discharge, it stays unsure whether physiologically raised degrees of calcitonin during pregnancy add to renal calcium discharge.

Additionally, this absorptive hypercalciuria refutes nomograms utilized fHypocalciuria during pregnancy has been connected to conditions, for example, toxemia, pregnancy-actuated hypertension, and serum calcitriol levels equivalent to those in non-pregnant people. These adjustments principally result from impeded renal capability and lessened creatinine leeway, instead of going about as causative variables for hypertension. In any case, calcium supplementation mitigates the gamble of toxemia among ladies with the least quintile of calcium consumption, highlighting the pathophysiological association between calcium digestion and pregnancy-actuated hypertension.or diagnosing familial hypocalciuric hypercalcemia during pregnancy. Albeit pharmacological portions of calcitonin upgrade renal

calcium discharge, it stays unsure whether physiologically raised degrees of calcitonin during pregnancy add to renal calcium discharge.

2.5 FACTORS AFFECTING CALCIUM AND PHOSPHORUS LEVELS

Several factors can influence the absorption, metabolism, and utilization of calcium and phosphorus, impacting maternal and fetal well-being. Understanding these factors is crucial for optimizing nutrient intake and maintaining mineral balance during pregnancy.

1. Hormonal Changes: Pregnancy hormones such as estrogen, progesterone, and calcitriol (active vitamin D) play key roles in regulating calcium and phosphorus metabolism (Kovacs, 2016). Hormonal fluctuations can affect intestinal absorption, renal reabsorption, and bone turnover of calcium and phosphorus, impacting mineral homeostasis.
2. Gestational Age: Calcium and phosphorus requirements may vary throughout pregnancy, with increased demands during the third trimester to support fetal skeletal mineralization and growth (Kovacs, 2016). Adequate intake of these minerals is essential to meet the needs of both the mother and the developing fetus.
3. Dietary Intake: The maternal diet significantly influences calcium and phosphorus levels during pregnancy. Consuming foods rich in these minerals, such as dairy products, leafy greens, nuts, seeds, and fish with edible bones, is essential for meeting nutrient requirements (National Institutes of Health, 2020).
4. Vitamin D Status: Adequate vitamin D levels are crucial for calcium absorption and utilization during pregnancy (Holick, 2007). Vitamin D deficiency can impair calcium metabolism and increase the risk of adverse pregnancy outcomes, emphasizing the importance of maintaining optimal vitamin D status.

5. Maternal Age: Maternal age may impact calcium and phosphorus metabolism during pregnancy. Younger pregnant individuals may have higher calcium requirements due to ongoing skeletal growth, while older individuals may be at increased risk of bone-related complications (Kovacs, 2016).
6. ccParathyroid Hormone Regulation: Parathyroid hormone (PTH) plays a key role in calcium and phosphorus homeostasis during pregnancy (Seely *et al.*, 1997). Dysregulation of PTH secretion can affect mineral balance and bone health, highlighting the importance of hormonal regulation.

7. Renal Function: Changes in renal function during pregnancy can influence calcium and phosphorus excretion and reabsorption (Kovacs, 2016). Adequate renal function is essential for maintaining mineral balance and preventing mineral imbalances or deficiencies.
8. Gastrointestinal Factors: Gastrointestinal factors such as nausea, vomiting, and gastrointestinal disorders can affect nutrient absorption and utilization during pregnancy (Kovacs, 2016). Managing gastrointestinal symptoms and ensuring adequate nutrient intake are essential for optimizing mineral status.
9. Medications and Supplements: Certain medications and supplements may interfere with calcium and phosphorus metabolism during pregnancy (Kovacs, 2016). Healthcare providers should carefully evaluate medication use and recommend appropriate supplementation to meet maternal and fetal nutrient needs.
10. Overall Health Status: Maternal health conditions such as gestational diabetes, preeclampsia, and thyroid disorders can impact calcium and phosphorus metabolism

(Kovacs, 2016). Managing underlying health conditions and monitoring mineral levels are essential for promoting maternal and fetal well-being.

All these factors, including hormonal changes, gestational age, dietary intake, vitamin D status, maternal age, parathyroid hormone regulation, renal function, gastrointestinal factors, medications, and overall health status, can influence calcium and phosphorus levels during pregnancy and should be considered when assessing maternal nutrient status and providing appropriate recommendations for optimizing mineral balance.

2.6 METHODS FOR MEASURING CALCIUM AND PHOSPHORUS LEVELS

Markers of bone turnover, which reflect bone arrangement and resorption, have been contemplated during pregnancy however present difficulties due to critical intra-and interindividual fluctuation. Issues with bone markers during pregnancy incorporate the absence of prepregnancy standard qualities, hemodilution, expanded glomerular filtration rate (GFR), adjusted creatinine discharge, commitments from placenta, uterus, and hatchling, debasement and leeway by the placenta, and absence of diurnally planned or abstained examples. While bone resorption markers (e.g., deoxypyridinoline, pyridinoline, and C-telopeptide) reliably show expanded levels from right on time or mid-pregnancy, bone arrangement markers (e.g., osteocalcin, procollagen I carboxypeptides, and bone-explicit soluble phosphatase) are for the most part diminished in ahead of schedule or mid-pregnancy yet transcend before term. Be that as it may, these bone arrangement markers are not normally revised for hemodilution or expanded GFR, possibly covering changes in bone development. Complete soluble phosphatase rises right off the bat in pregnancy because of

the placental division and is certainly not a helpful marker of bone development during pregnancy.

Restricted bone biopsy information and aftereffects of bone turnover markers propose expanded bone resorption from as soon as the tenth seven day stretch of pregnancy, while bone arrangement might be smothered or typical, contingent upon marker rectification. Remarkably, there is negligible maternal-fetal calcium move in the principal trimester, and there is no undeniable expansion in turnover markers during the third trimester when maternal-fetal calcium move tops. These discoveries propose that maternal skeletal resorption assumes a minor part in calcium homeostasis during pregnancy, with upregulated gastrointestinal calcium retention being the essential component to fulfill fetal calcium needs.

Evaluating maternal skeletal commitment to calcium guideline during pregnancy by means of bone mineral substance or thickness concentrates on presents difficulties because of puzzling elements like changes in body sythesis, weight, and skeletal volumes. Longitudinal examinations utilizing single and double photon absorptiometry (SPA and DPA) methods tracked down no huge change in areal bone thickness (aBMD) during pregnancy. Nonetheless, later examinations utilizing double energy X-beam absorptiometry (DXA) show unassuming abatements in aBMD at different skeletal locales post-pregnancy, however changes are little and not clinically huge for individual ladies. Ultrasound concentrates on report diminishes in files relating with volumetric bone mineral thickness (BMD) at the os calcis and fingers during pregnancy, however the dependability and importance of these discoveries stay dubious. In spite of these changes, pregnancy doesn't hinder skeletal strength or lead to diminished bone thickness in the long haul, as confirmed by epidemiological examinations showing no critical relationship among equality and bone thickness or break risk.

2.7 IMPLICATION OF IMBALANCED CALCIUM AND PHOSPHORUS LEVELS.

1)Pseudohyperparathyroidism

As delineated earlier, pseudohyperparathyroidism manifests as hypercalcemia instigated by the physiological release of parathyroid hormone-related protein (PTHrP), leading to heightened skeletal resorption. This mechanism mirrors how PTHrP also induces hypercalcemia in cases of malignancy. An illustrative instance involved the mammary glands as the source of PTHrP, as evidenced by persistent hypercalcemia and elevated PTHrP levels until bilateral reduction mammoplasty was performed. Notably, this phenomenon has been observed in women with enlarged breasts. Another scenario demonstrated the reversal of hypercalcemia, elevated PTHrP, and suppressed parathyroid hormone (PTH) levels shortly after an urgent cesarean section, thereby confirming the placenta as the origin. In all instances of pseudohyperparathyroidism, it is prudent to anticipate elevated cord blood calcium levels, posing a risk for fetal and neonatal hypoparathyroidism with accompanying hypocalcemic tetany in the newborn.

TREATMENT CONSIDERATIONS

The diagnosis might remain uncertain until postpartum, when serum calcium levels promptly return to normal (suggesting placental PTHrP as the etiology) or remain elevated (suggesting mammary gland production of PTHrP). Preceding delivery, the medical approach resembles that of primary hyperparathyroidism.

2) Primary Hyperparathyroidism

This condition is intriguing, with restricted information accessible in regards to its commonness. Hypercalcemia has been recognized in around 0.03% of regularly screened ladies of regenerative age, while two case series demonstrated that 1% of all parathyroidectomies were performed during pregnancy. Various cases have been reported in

the clinical writing. Analysis might be trying because of the typical physiological changes prompted by pregnancy, which lower complete serum calcium levels and stifle parathyroid chemical (PTH). Notwithstanding, raised ionized or egg whites rectified calcium levels, alongside noticeable PTH, normally show essential hyperparathyroidism. Pregnancy-related physiological changes, as depicted prior, increment digestive calcium retention, bone resorption, and hypercalciuria, possibly worsening essential hyperparathyroidism and prompting more serious hypercalcemia, pancreatitis, and kidney stones. Notwithstanding, the dynamic exchange of calcium across the placenta to the creating embryo halfway balances the gamble of deteriorating hypercalcemia.

Essential hyperparathyroidism during pregnancy has been related with vague side effects like those of ordinary pregnancy, including sickness, regurgitating, renal colic, discomfort, and muscle throbs. In any case, it is connected to an unsettling pace of unfavorable results in the hatchling and child, including unconstrained fetus removal, stillbirth, perinatal passing, and neonatal tetany. Later case series recommend lower paces of unfriendly results contrasted with more seasoned writing, yet the dangers stay huge. Careful remedy during the subsequent trimester is generally prescribed to forestall these unfavorable results. Elective medical procedure has been demonstrated to be very much endured and altogether diminishes the occurrence of unfriendly occasions contrasted with clinical administration. Picking the subsequent trimester considers fetal organogenesis to be finished and mitigates the dangers related with a medical procedure during the third trimester.

While moderate administration of gentle, asymptomatic essential hyperparathyroidism during pregnancy has been effective, confusions can in any case happen. Hence, without authoritative information, medical procedure during the subsequent trimester stays the standard proposal. Albeit late examinations propose lower paces of unfriendly results, the

potential for fast and extreme post pregnancy compounding of hypercalcemia, known as "parathyroid emergency," highlights the significance of watchful administration and follow-up care.

TREATMENT CONSIDERATIONS

The essential thought spins around the choice of whether to carry out elective procedure during the subsequent trimester or to screen the patient with the assumption for deferring careful mediation until after conveyance. Conclusive clinical administration rules for hyperparathyroidism during pregnancy are missing, with the essential spotlight being on guaranteeing satisfactory hydration and amending electrolyte irregularities. Pharmacological specialists for treating hypercalcemia have not gone through adequate concentrate in pregnancy, and circle back to youngsters has been restricted. Calcitonin, which doesn't cross the placenta, has been used securely. Oral phosphate organization has additionally been endeavored; be that as it may, it is blocked by unfriendly impacts like loose bowels, hypokalemia, and the gamble of delicate tissue calcifications. Bisphosphonates are moderately contraindicated because of their likely unfavorable consequences for fetal endochondral bone turn of events, albeit a survey of 78 cases tracked down no undeniable issues in many occasions. Denosumab, which crosses the placenta and has been displayed to prompt an osteopetrotic-like aggregate in fetal cynomolgus monkeys and rodents, ought to be stayed away from during human pregnancy. High-portion magnesium has been proposed as an elective treatment that might diminish serum PTH and calcium levels by enacting the calcium-detecting receptor, however its adequacy for this reason has not been adequately examined. Cinacalcet, a calcium receptor agonist used to stifle PTH and calcium in nonpregnant people with essential or optional hyperparathyroidism and parathyroid carcinoma, has been explored different avenues regarding during pregnancy. Nonetheless,

because of the declaration of the calcium receptor in the placenta and its guideline of fetal-placental calcium move, concerns continue with respect to likely unfriendly impacts of cinacalcet on the hatchling and youngster. Without heparin hemodialysis can decrease serum calcium levels before a medical procedure.

In cases oversaw therapeutically, parathyroidectomy is encouraged to be performed post pregnancy, with close observing to recognize any post pregnancy hypercalcemic emergency. Considering that these ladies regularly present very early in life with essential hyperparathyroidism, hereditary testing might be justified to bar acquired causes.

3) Vitamin D Deficiency and Insufficiency

Far reaching examinations concerning the impacts of lack of vitamin D or inadequacy on human pregnancy are inadequate. Nonetheless, existing information from little clinical preliminaries of vitamin D supplementation, observational examinations, and case reports propose that, in accordance with creature studies, vitamin D inadequacy and lack don't compound maternal calcium homeostasis. Maternal hypocalcemia will in general be milder in instances of lack of vitamin D because of the impacts of auxiliary hyperparathyroidism, which increments skeletal resorption and renal calcium reabsorption. Subsequently, hypocalcemia coming about because of lack of vitamin D has not been absolutely connected to the antagonistic fetal results related with maternal hypoparathyroidism.

The fetal impacts of lack of vitamin D, including the failure to shape calcitriol and the shortfall of the vitamin D receptor, have been examined across a few creature animal varieties. These examinations reliably show that the hatchling keeps up with ordinary serum calcium levels and accomplishes full skeletal mineralization at term. Neonatal hypocalcemia and rickets might happen in newborn children brought into the world to moms with serious

lack of vitamin D, normally showing a long time to months after birth when gastrointestinal calcium retention becomes reliant upon calcitriol.

Various examinations have investigated potential extraskeletal benefits related with third-trimester estimations of 25OHD or assessed vitamin D admissions during pregnancy or the primary year post pregnancy. These examinations have conflictingly connected vitamin D status to advantages, for example, diminished bacterial vaginosis, toxemia, preterm conveyance, lower frequency of type 1 diabetes, and upgraded skeletal mineralization in posterity. Nonetheless, these affiliations are puzzled by factors adding to bring down 25OHD levels, like maternal overweight/heftiness, lower financial status, unfortunate nourishment, and absence of activity. Randomized clinical preliminaries looking at higher versus lower admissions of vitamin D during pregnancy are important to approve these affiliations. By and by, the aftereffects of associational investigations don't legitimize endorsing higher vitamin D admissions during pregnancy to forestall these estimated results.

Albeit various clinical preliminaries of vitamin D supplementation have been led, a couple have included more than 100 review members who were vitamin D insufficient at benchmark. Among these preliminaries, mediations regularly elaborate fake treatment/no treatment versus low or high-portion vitamin D supplementation started before mid-pregnancy and went on until conveyance. While vitamin D supplementation reliably expanded maternal and line blood 25OHD levels, there was no general impact on rope blood calcium. Besides, no critical obstetrical or fetal advantages were seen in many examinations, regardless of varieties in concentrate on plan and member attributes.

Methodical surveys analyzing the impact of vitamin D supplementation during pregnancy on maternal, fetal, and neonatal results have yielded uncertain outcomes. While certain surveys recommend a potential decrease in the gamble of toxemia with consolidated vitamin D and

calcium supplementation, the general proof remaining parts lacking to presume that vitamin D supplementation during pregnancy gives obstetrical advantages, especially comparable to calcium and bone digestion. In any case, continuous premium continues examining whether vitamin D forestalls antagonistic non-skeletal occasions in both mother and child. In the meantime, guaranteeing vitamin D adequacy in pregnant ladies before or from the get-go in pregnancy is suggested.

TREATMENT CONSIDERATIONS

Vitamin D supplementation represents no mischief to nonpregnant grown-ups except if over the top portions prompting hypervitaminosis D are controlled (regularly surpassing 10,000 IU day to day). Be that as it may, the most extreme degree of maternal admission considered alright for the creating embryo stays unsure. Clinical preliminaries including pregnant ladies have securely used portions going from 400 to 5,000 IU of vitamin D day to day without obvious antagonistic consequences for either the mother or the posterity. It is prudent for all pregnant ladies to streamline their vitamin D admission. This training effectively mitigates any nonskeletal results related with lack of vitamin D and guarantees that babies have satisfactory vitamin D stores to standardize mineral homeostasis in the progress from placental reliance to gastrointestinal assimilation of minerals from milk during the underlying hours to days after birth.

4) Hypoparathyroidism

Hypoparathyroidism during pregnancy typically manifests as a pre-existing condition that poses a challenge for clinicians to effectively manage. The clinical course of hypoparathyroidism during pregnancy is complex, as evidenced by seemingly contradictory case reports in the literature [reviewed in]. In the early stages of pregnancy, some women

with hypoparathyroidism experience fewer symptoms of hypocalcemia and require less supplemental calcium. This observation suggests a limited role for parathyroid hormone (PTH) in pregnant individuals, indicating a potential increase in calcitriol levels and/or enhanced intestinal calcium absorption in the absence of PTH. However, other reports indicate that certain pregnant women with hypoparathyroidism necessitate increased replacement of calcitriol to prevent worsening hypocalcemia. Complicating matters further, some case reports suggest that the normal decrease in total serum calcium levels during pregnancy prompts treatment with increased calcium and calcitriol supplementation. Fewer cases cite dose adjustments in calcitriol and calcium due to maternal symptoms of hypocalcemia or tetany, or objective evidence of true hypocalcemia (low ionized or albumin-corrected calcium).

Late cases highlight the fluctuation over hypoparathyroidism during pregnancy, for certain people encountering improvement, deteriorating, or steadiness of the condition. Anticipating who will encounter improvement or weakening during pregnancy stays testing; the essential goal is to keep up with egg whites revised serum calcium or ionized calcium inside the typical reach all through pregnancy. Maternal hypocalcemia coming about because of hypoparathyroidism should be stayed away from, as it has been connected to intrauterine fetal hyperparathyroidism and fetal destruction. Then again, over-treatment ought to be stayed away from, as maternal hypercalcemia is related with fetal and neonatal entanglements saw in essential hyperparathyroidism. Given their more limited half-lives, lower hazard of harmfulness, and broad clinical use, calcitriol and 1α-calcidiol are suggested for supplementation.

In late pregnancy, hypoparathyroid ladies might encounter hypercalcemia except if the dose of calcitriol and supplemental calcium is considerably diminished or ceased. This peculiarity

is by all accounts interceded by expanding levels of parathyroid chemical related protein (PTHrP) in maternal dissemination during late pregnancy. On the other hand, a case report of hypoparathyroidism during pregnancy noticed a transient time of expanded calcitriol necessity promptly post-conveyance, before lactation was completely settled. This peculiarity might originate from the end of placental PTHrP creation, trailed by a flood in PTHrP creation by the lactating breast.

TREATMENT CONSIDERATIONS

During pregnancy, it is fitting to keep up with the egg whites revised serum calcium inside the mid-typical reach to guarantee satisfactory calcium conveyance to the hatchling. This quick term proposal separates from the common idea for non-pregnant grown-ups, which intends to keep up with the egg whites amended serum calcium close or somewhat underneath the lower furthest reaches of typical. This approach lessens the renal sifted load and may possibly sluggish the movement of nephrocalcinosis over the long haul. As examined beforehand, the board during pregnancy might include keeping up with prior portions of calcium, calcitriol, or 1α-calcidiol unaltered, or it might require changes, either up or descending, in both calcium and the dynamic vitamin D analog.

5) Pseudohypoparathyroidism

Pseudohypoparathyroidism, a hereditary problem portrayed by protection from parathyroid chemical (PTH), gives side effects of hypocalcemia, hypophosphatemia, and raised PTH levels. The problem envelops two essential subtypes: type I, portrayed by lessened PTH-actuated phosphaturia and cyclic AMP creation in the kidneys, and type II, which presentations dulled PTH-prompted phosphaturia solely. The board of both subtypes matches that of hypoparathyroidism.

The reported involvement in pseudohypoparathyroidism during pregnancy intently reflects that of hypoparathyroidism, with cases showing shifting levels of progress, decay, or solidness. In occasions of type I pseudohypoparathyroidism, four pregnancies exhibited improvement, set apart by lessened hypocalcemic side effects, fulfillment of normocalcemia, decrease of PTH levels to approach typical, a few overlap expansions in calcitriol levels, standardization of urinary calcium discharge, and end of supplemental vitamin D, calcitriol, or analogs. These perceptions recommend PTH-autonomous upgrades in digestive calcium assimilation and calcitriol union during pregnancy, thus further developing calcium homeostasis. Quite, endogenous serum calcitriol levels multiplied by mid-pregnancy in two situations where supplemental calcitriol had been stopped. Alternately, seven different pregnancies including ladies with types I and II pseudohypoparathyroidism revealed abstract deteriorating of hypocalcemia-like side effects or the need to raise dosages of calcium, calcitriol, or 1α-calcidiol. A new case recorded no prerequisite for changes in calcium or calcitriol measurements during pregnancy.

Tireless maternal hypocalcemia during pregnancy in instances of pseudohypoparathyroidism can hasten unfavorable fetal results likened to those related with maternal hypoparathyroidism, including parathyroid hyperplasia, skeletal demineralization, and cracks. Support of maternal calcium fixation inside the typical reach is basic to hinder these fetal confusions.

TREATMENT CONSIDERATIONS

Support the egg whites remedied serum calcium inside the mid-ordinary reach. Like hypoparathyroidism, accomplishing this objective might involve keeping up with prior portions of calcium, calcitriol, or 1α-calcidiol unaltered, or require changes, either upwards or downwards, in both calcium and the dynamic vitamin D analog.

6) **Osteoporosis in Pregnancy** The occasional occurrence of fragility fractures, typically vertebral or appendicular, during the third trimester or puerperium, may prompt subsequent confirmation of low bone mineral density through DXA scans. In many cases, a pre-pregnancy BMD evaluation is inaccessible, as it is considered normal not considered significant in sound regenerative age ladies. Subsequently, the degree of bone misfortune during pregnancy stays unsure much of the time, leaving open the likelihood that low bone thickness or skeletal delicacy originates before pregnancy. Proof recommending a hereditary inclination comes from reports demonstrating a higher pervasiveness of delicacy cracks among moms of ladies with pregnancy-related osteoporosis. It is conceivable that pregnancy might prompt huge skeletal misfortunes in specific people, inclining them toward cracks. Pregnancy-actuated changes in mineral digestion, including expanded bone resorption, combined with variables like low dietary calcium admission and vitamin D inadequacy, may add to skeletal misfortunes. Besides, raised bone turnover rates, a realized gamble factor for delicacy breaks beyond pregnancy, may additionally elevate crack gamble during growth. Observational examinations have revealed expanded bone resorption during pregnancy, proposing a likely connection to delicacy cracks.

Osteoporosis related with pregnancy is probable under-perceived and under-detailed, with numerous vertebral pressure cracks slipping by everyone's notice clinically. Symptoms such as back pain, often dismissed as a common pregnancy-related complaint, may indicate vertebral fractures, but their significance may be overlooked. While the literature predominantly highlights cases of multiple compression fractures, the incidence of single vertebral compression fractures during pregnancy remains uncertain. Although emphasis is often placed on vertebral compression fractures, some reports suggest that fractures of the ankle and other lower limbs may be more prevalent. Osteoporosis typically manifests during the first pregnancy, with subsequent pregnancies or higher parity not necessarily increasing

the risk. This recommends that reversible variables, like healthful inadequacies, may have been redressed after the underlying pregnancy, or that compromised vertebrae fell under the type of the principal pregnancy. Patients generally present with lower thoracic or lumbar agony, which can be incapacitating because of vertebral breakdown. While most cases show ordinary serum sciences and calciotropic chemical levels, some might uncover optional reasons for bone misfortune. These can incorporate low calcium admission, anorexia nervosa, celiac illness, hyperparathyroidism, osteogenesis imperfecta, hereditary transformations, untimely ovarian disappointment, and certain drugs. Torment from vertebral pressure cracks normally settle immediately more than half a month, corresponding with significant upgrades in bone thickness post-pregnancy. Recurrence of fractures in subsequent pregnancies is rare. Hence, while various medical and surgical interventions have been employed in isolated cases, the tendency for spontaneous improvement makes pharmacological treatment generally unwarranted, except in severe cases. Waiting 12-18 months post-pregnancy to assess the extent of BMD recovery after a vertebral fracture may be prudent. Another distinct condition, focal transient osteoporosis of the hip, is rare, self-limiting, and likely not a consequence of altered hormone levels or mineral balance during pregnancy. Instead, it may result from local factors such as femoral venous stasis, nerve pressure, or trauma. Patients typically present with hip pain, limping, or hip fractures in the third trimester or postpartum period. Radiological and MRI findings confirm reduced bone density and increased water content in the affected femoral head and neck. Symptoms and radiological changes typically resolve within months postpartum, with conservative measures often sufficient during the symptomatic phase. However, fractures may necessitate urgent intervention. Recurrence occurs in about 40% of cases, prompting prophylactic hip arthroplasty in select cases. Vertebral compression fractures and transient osteoporosis of the hip may overlap in some

cases during pregnancy, highlighting the complex interplay of factors contributing to skeletal fragility during gestation.

TREATMENT CONSIDERATIONS

In cases of fragility fractures associated with pregnancy, treatment strategies typically involve optimizing calcium and vitamin D intake, promoting appropriate weight-bearing physical activities, addressing any nutritional deficiencies, and managing reversible causes of bone loss or fragility. Short-term pain relief may be achieved with the use of supportive corsets. While breastfeeding is not contraindicated, it's essential to discuss its relative safety, considering its potential impact on bone mineral density (BMD) loss and transiently increased fracture risk. It's important to exercise caution with pharmacotherapy, as spontaneous BMD recovery of 20-70% typically occurs within six to twelve months in women who fractured but received no specific interventions. Therefore, it's advisable to delay pharmacotherapy for 12-18 months to assess the extent of spontaneous recovery. Various pharmacotherapies, including calcitonin, bisphosphonates, denosumab, strontium ranelate, and teriparatide, have been documented, often following regimens similar to those used for post-menopausal osteoporosis, with treatment terms going from a half year to as long as 10 years. Nonetheless, these reports are observational and need controls to decide if the noticed upgrades in BMD surpass those normal with unconstrained recuperation. Vertebroplasty and kyphoplasty have additionally been utilized to oversee excruciating vertebral cracks post pregnancy, in spite of the fact that their general adequacy stays dubious, as randomized preliminaries have not in every case exhibited predominance over hoax a medical procedure or clinical mediations in more seasoned subjects.

In cases of transient osteoporosis of the hip without resultant fracture, the primary consideration revolves around whether to proceed with prophylactic rodding of the affected

femur(s) or to adopt a watchful waiting approach with the expectation of complete spontaneous recovery.

7) Familial Hypocalciuric Hypercalcemia (FHH)

Inactivating transformations influencing the calcium-detecting receptor lead to this autosomal prevailing condition described by hypercalcemia and hypocalciuria. All through pregnancy, tireless hypercalcemia is seen close by non-stifled parathyroid chemical (PTH) levels, with serum calcium levels possibly expanding continuously across the trimesters. In spite of essential hyperparathyroidism, partial discharge of calcium stays unaltered during pregnancy in this condition, as the physiological expansion in digestive calcium retention abrogates it, prompting hypercalciuria. Consequently, familial hypocalciuric hypercalcemia (FHH) presenting during pregnancy may be mistakenly diagnosed as primary hyperparathyroidism. Regrettably, there have been instances where pregnant individuals with FHH were misdiagnosed with primary hyperparathyroidism due to worsening hypercalcemia and hypercalciuria. In one case, a lady went through a parathyroidectomy including three-and-a-half organs during the second trimester before FHH was accurately distinguished, as her hypercalcemia persevered, and her youngster was likewise observed to be hypercalcemic.

Pregnancy for ladies with familial hypocalciuric hypercalcemia regularly advances without huge entanglements for the mother. Notwithstanding, maternal hypercalcemia can bring about the concealment of fetal and neonatal parathyroid capability, prompting tetany in both typical and hemizygous babies. While a hemizygous youngster may later foster harmless hypercalcemia, the presence of two inactivating changes in the calcium receptor (normally acquired from the two guardians who are hemizygous for FHH) may encourage a dangerous hypercalcemic emergency in the child.

TREATMENT CONSIDERATIONS

Elevated calcium levels are a typical occurrence in women with FHH, and there is no need to intervene or confuse it with primary hyperparathyroidism. Rather, close monitoring of the newborn is essential to detect any postnatal hypocalcemia and to observe for subsequent hypercalcemia, which could indicate inheritance of the mutation.

8) Genetic Vitamin D Resistance Syndromes

Case reports and series have revealed insight into the effect of pregnancy on hereditary problems connected with nutrient digestion. For the most part, pregnancies in ladies with vitamin D-subordinate rickets type 1 (VDDR-I), brought about by the shortfall of Cyp27b1, and in those with VDDR-II, coming about because of the shortfall of useful VDRs, have been to a great extent ordinary. In a particular instance of a uninteresting VDR-II pregnancy, the lady kept up with her pre-pregnancy admission of supplemental calcium (800 mg) and high-portion calcitriol, with her clinicians later changing the calcitriol portion during pregnancy "in light of the information that the circling 1,25-(OH)2D focus regularly ascends during pregnancy," as opposed to because of any adjustment of egg whites changed serum calcium. Thusly, the need of this change stays hazy. Nonetheless, it could be sensible to build the calcitriol portion to match the typical pregnancy-prompted increment. In ladies with VDDR-I, the calcitriol portion stayed unaltered in 33% of pregnancies yet expanded by 1.5 to 2-crease in others.

TREATMENT CONSIDERATIONS

Keep an ordinary egg whites rectified serum calcium with acclimations to oral calcium and calcitriol dosing case by case in view of sequential checking of blood sciences.

9) 24-Hydroxylase Deficiency

In non-pregnant grown-ups, the shortfall of the catabolic impacts of 24-hydroxylase prompts raised calcitriol levels and gentle hypercalcemia, which might stay asymptomatic. Nonetheless, during pregnancy, the physiological expansion in calcitriol, which commonly goes from 2 to 5-overlay, is unobstructed by catabolism. This outcomes in a misrepresented ascent in calcitriol levels, prompting suggestive hypercalcemia. The hypercalcemia can be articulated, joined by smothered or imperceptible degrees of PTH, and raised calcitriol fixations outperforming the normal reach for pregnancy. Pregnant people may likewise give complexities like nephrolithiasis or intense pancreatitis.

TREATMENT CONSIDERATIONS

Overseeing hypercalcemia during pregnancy presents difficulties because of the restricted accessibility of supported remedial specialists for use in pregnant ladies. The essential guilty party is expanded gastrointestinal calcium ingestion, proposing that intercessions, for example, upgraded hydration, a respectably confined calcium diet, and phosphate supplementation to sequester dietary calcium are somewhat protected systems. Should PTH levels transcend ordinary, acclimations to dietary calcium limitation might be important to forestall maternal bone resorption and fetal auxiliary hyperparathyroidism. Pharmacological mediations ought to be held for serious cases and utilized mindfully. Choices incorporate oral glucocorticoids to restrain digestive calcium retention, circle diuretics, calcitonin, and bisphosphonates; be that as it may, denosumab ought to be stayed away from because of noticed teratogenic impacts in creature studies. Cinacalcet is probably not going to be viable since PTH levels are now stifled by the joined impacts of pregnancy and hypercalcemia.

10) Low or High Calcium Intake

During pregnancy, the multiplying of digestive calcium ingestion empowers ladies to adjust to changing calcium admissions, guaranteeing the satisfaction of fetal calcium requests. While incredibly low maternal calcium admission could possibly disturb maternal calcium homeostasis and fetal mineral gathering, clinical proof investigating this chance remaining parts scant. Among ladies with low dietary calcium consumption, concentrates on yield blended results in regards to the viability of calcium supplementation during pregnancy in working on maternal or neonatal bone thickness. Momentary proof proposes that bone turnover markers decline with the organization of 1.2 grams of supplemental calcium for 20 days to pregnant Mexican ladies with mean dietary calcium admission of 1 gram. In a twofold visually impaired study including 256 pregnant ladies, 2 grams of calcium supplementation just improved bone mineral substance in babies of enhanced moms with the most reduced quintile of calcium consumption. A few instances of delicacy breaks happening during pregnancy include ladies with extremely low calcium admissions (<300 mg each day), requiring significant maternal skeletal resorption to meet fetal calcium prerequisites and keep up with maternal serum calcium levels.

For the most part, the physiological changes in calcium and bone digestion during pregnancy and lactation probably get the job done for fetal bone development and bosom milk creation in ladies with sensibly sufficient calcium admission. Notwithstanding, enhancing calcium for pregnant ladies with low calcium admission can be legitimate by relationship between low calcium consumption and both toxemia and posterity hypertension. Clinical preliminaries and meta-examinations have shown that calcium supplementation decreases toxemia risk in ladies with low dietary calcium admissions, yet not in those with adequate admission.

Inordinate calcium consumption, similar to essential hyperparathyroidism, can prompt uplifted gastrointestinal calcium ingestion, maternal hypercalcemia, expanded transplacental

calcium stream, and concealment of fetal parathyroids. Occasions of neonatal hypoparathyroidism have been archived in ladies consuming 3 to 6 grams of basic calcium everyday as acid neutralizers or enemies of nauseants.

TREATMENT CONSIDERATIONS

Extremely low calcium consumption should be kept away from on the grounds that it builds the gamble of toxemia, maternal skeletal resorption, and deficient mineralization of the fetal skeleton. Alternately, high calcium admission should be kept away from in light of the fact that it expands the gamble of maternal hypercalcemia and concealment of the fetal parathyroids. The Foundation of Medication exhorts that pregnant ladies require similar calcium consumption as non-pregnant ladies, a worth that reaches from 1,000 to 1,200 mg day to day, contingent upon age.

11) Hypercalcemia of Malignancy

Hypercalcemia of threat is normally a terminal condition. At the point when it has been analyzed during pregnancy, at times the child has been saved from chemotherapy, though in different cases the pregnancy was ended (or overlooked) so chemotherapy could be regulated trying to draw out the lady's life. A big part of distributed case reports haven't even referenced the child's result. A child brought into the world of a mother with humoral hypercalcemia of harm might have a high centralization of calcium in line blood, and is at high gamble for fetal and neonatal hypoparathyroidism with hypocalcemic tetany.

12) FGF-23 Disorders

X-connected hypophosphatemic rickets (XLH) emerges from inactivating transformations in the PHEX quality, prompting raised coursing levels of FGF23, which in this way actuate

hypophosphatemia joined by rickets or osteomalacia. Concentrates on in a mouse model of XLH uncovered uninteresting pregnancies. Notwithstanding extraordinarily raised flowing FGF23 levels, commonly connected with decreased calcitriol blend and upgraded catabolism, maternal serum calcitriol levels expanded to the run of the mill undeniable levels saw during pregnancy. This flood in calcitriol ought to work with expanded assimilation of gastrointestinal calcium and phosphate. While a few case reports have recorded supported hypophosphatemia during pregnancy in ladies with XLH, no unfriendly results have been accounted for. By the by, it is by and large prescribed to control calcitriol and phosphate supplementation to keep up with serum phosphate levels near ordinary during pregnancy.

Hyperphosphatemic problems originating from disabled FGF23 capability have not been investigated during human pregnancy, and information from creature models are missing because of lethality before sexual development in impacted conditions. Hyperphosphatemia coming about because of renal inadequacy or disappointment is related with expanded dangers of gestational hypertension, toxemia, eclampsia, and maternal mortality, as proven by both creature and human investigations. Nonetheless, the exact commitment of hyperphosphatemia to these dangers stays questionable.

TREATMENT CONSIDERATIONS

With regards to XLH and different problems intervened by FGF-23, coming about in hypophosphatemia, keeping up with serum phosphate levels near ordinary is suggested through the organization of phosphate supplements and, if essential, calcitriol. Burosumab, an original enemy of FGF23 neutralizer, really revises hypophosphatemia in different FGF-23 interceded messes; in any case, its wellbeing and viability during pregnancy stay neglected.

Regarding hyperphosphatemic disorders arising from insufficient FGF23 action, there is a lack of data to inform potential treatment strategies. Nonetheless, cautious use of phosphate binders may be beneficial, with careful consideration to avoid any that could pose harm to the fetus.

2.8 CONCLUSION AND RECOMMENDATION

Balancing calcium and phosphate levels during pregnancy involves ensuring adequate dietary intake, considering supplementation when necessary, maintaining a balanced ratio of calcium to phosphorus, optimizing calcium absorption, limiting phosphorus-rich additives, and staying hydrated. These recommendations support maternal and fetal health by promoting proper bone development and mineral metabolism during pregnancy.

1. Dietary Intake: Consume a balanced diet rich in calcium and phosphorus-rich foods. Good sources of calcium include dairy products, leafy greens, fortified foods, and fish with edible bones (National Institutes of Health, 2020). Phosphorus-rich foods include meat, poultry, fish, eggs, dairy products, nuts, and seeds (National Institutes of Health, 2020).
2. Supplementation: If dietary intake alone is insufficient to meet the recommended daily intake of calcium and phosphorus during pregnancy, consider supplementation under the guidance of a healthcare provider (Kovacs, 2001). Prenatal vitamins containing calcium and phosphorus may be prescribed to ensure adequate nutrient intake (Kovacs, 2001).
3. Calcium-to-Phosphorus Ratio: Aim for a balanced ratio of calcium to phosphorus in the diet. While the optimal ratio may vary, maintaining a ratio close to 1:1 is generally recommended for promoting bone health and mineral balance (Taljaard *et al.*, 2003).

Consuming foods with a balanced calcium-to-phosphorus ratio helps prevent mineral imbalances and supports proper bone development.

4. Calcium Absorption Enhancers: Increase the absorption of calcium by consuming foods rich in vitamin D, which enhances intestinal calcium absorption (Holick, 2007). Sources of vitamin D include fortified dairy products, fatty fish, eggs, and exposure to sunlight (Holick, 2007). Adequate vitamin D levels are essential for calcium utilization and bone mineralization during pregnancy.
5. Limit Phosphorus-Rich Additives: Avoid excessive consumption of processed foods and beverages containing phosphorus-rich additives such as phosphoric acid (Uribarri *et al.*, 2011). These additives, commonly found in sodas and processed meats, can disrupt calcium-phosphorus balance and may adversely affect bone health (Uribarri *et al.*, 2011).
6. Hydration: Maintain adequate hydration to support renal function and facilitate the excretion of excess phosphorus (Schrier *et al.*, 2008). Drinking plenty of water throughout the day helps prevent the accumulation of phosphorus in the body and promotes urinary excretion, contributing to mineral balance.

CHAPTER THREE

MATERIALS AND METHODS

3.0 Materials

The following materials were used during the research study;

1. EDTA containers
2. Lithium heparin container
3. Syringe (2ml and 5ml)
4. Cotton wool
5. Methylated spirit
6. Tourniquet
7. Gloves
8. Nose mask
9. Steel plates
10. Measuring tape
11. Body weight scale

PROCEDURE

1. Preparation:

- Wash your hands thoroughly to prevent contamination.
- Gather all the necessary equipment including gloves, alcohol swabs, tourniquet, blood collection tubes (with or without anticoagulants), and a needle.

2. Patient Preparation:

- Inform the patient about the procedure and ensure their consent.
- Position the patient comfortably, typically seated or lying down with their arm extended and palm facing upward.

3. Identification:

- Confirm the patient's identity by checking their ID bracelet or asking for their full name and date of birth.

4. Prepare the Site:

- Choose a suitable site for venipuncture, usually the antecubital vein on the inside of the elbow.

- Apply a tourniquet a few inches above the intended puncture site to make the veins more visible and easier to access.

5. Disinfection:

- Clean the skin over the puncture site with an alcohol swab and allow it to air dry. This helps to reduce the risk of contamination.

6. Needle Insertion:

- Once the site is prepared, use a sterile needle to puncture the vein at a slight angle.

- Once blood flow is established, remove the tourniquet.

7. Blood Collection:

- Collect the required amount of blood into the appropriate blood collection tube. Tubes for calcium measurement may or may not contain anticoagulants, depending on the specific test requirements.

8. Labeling:

- Label the blood collection tube with the patient's name, date, and time of collection to ensure proper identification and tracking.

9. Post-Collection Care:

- Apply pressure to the puncture site with a cotton ball or gauze to stop bleeding.

- Dispose of the used needle and other sharps in an appropriate sharps container.

- Instruct the patient to apply pressure to the site if bleeding persists and to avoid heavy lifting or strenuous activity with the arm for a short period.

10. Transportation:

- Ensure proper storage and transportation of the blood sample to the laboratory for analysis. Follow any specific instructions for sample handling and transportation to maintain sample integrity.

11. Analysis:

- The blood sample is analyzed in the laboratory using various methods to determine the concentration of calcium ions present in the blood.

3.1) METHOD FOR MEASURING BLOOD CALCIUM CONCENTRATION

The most common method used to analyze blood calcium levels is through a laboratory test known as a "serum calcium test." There are two main types of serum calcium tests: total calcium test and ionized calcium test.

1. Total Calcium Test: This test measures the total amount of calcium in the blood, including both ionized calcium (the physiologically active form) and calcium bound to proteins such as albumin. The total calcium test is typically performed using colorimetric or spectrophotometric methods.

2. Ionized Calcium Test: This test specifically measures the concentration of ionized calcium in the blood, which represents the biologically active form of calcium that is freely available for physiological processes. Ionized calcium testing is often done using ion-selective electrodes or ion-specific electrodes, which directly measure the concentration of free calcium ions in the blood.

Both types of tests provide valuable information about calcium levels in the blood.

The total calcium test is a common laboratory test used to measure the total concentration of calcium in the blood. Here's how the total calcium test is carried out:

1 Processing:

- If the blood sample contains an anticoagulant, it may need to be centrifuged to separate the plasma (or serum) from the cellular components of the blood. Plasma or serum can be used for the total calcium test.

2 Analytical Method:

- The total calcium test is typically performed using colorimetric or spectrophotometric methods. These methods rely on chemical reactions that produce a color change in proportion to the amount of calcium present in the sample.

3. Reagents:

- Reagents are added to the plasma or serum sample to initiate the chemical reaction. These reagents may include a dye or indicator solution that reacts with calcium ions to produce a measurable color change.

4 Measurement:

- The absorbance or intensity of the color produced is measured using a spectrophotometer. This instrument quantifies the amount of light absorbed by the sample at a specific wavelength, allowing for the calculation of the calcium concentration.

5 Calibration:

- Before analyzing patient samples, the spectrophotometer is calibrated using standard solutions with known concentrations of calcium. This calibration ensures the accuracy and reliability of the test results.

6. Calculation:

- The concentration of calcium in the patient's blood sample is determined based on the absorbance or intensity of the color reaction, using a calibration curve generated from the standard solutions.

7 Reporting Results:

- The test results are reported in units of measurement such as milligrams per deciliter (mg/dL) or millimoles per liter (mmol/L) of calcium in the blood.

8. Interpretation:

- The test results are interpreted by healthcare professionals in the context of the patient's medical history, symptoms, and overall health status. Abnormalities in total calcium levels may indicate various medical conditions that require further evaluation and management.

3.2) METHOD FOR MEASURING BLOOD PHOSPHATE CONCENTRATION

The method commonly used to analyze blood phosphate levels is called the "phosphate assay" or "phosphorus assay." There are several laboratory methods available for measuring phosphate levels in blood, and the choice of method may depend on factors such as the laboratory's equipment, resources, and specific requirements. Some of the commonly used methods include:

1. Colorimetric Method: This method relies on the formation of a colored complex between phosphate ions and a reagent, which can be measured spectrophotometrically. The intensity of the color is proportional to the concentration of phosphate in the sample. Various reagents can be used for this purpose, such as ammonium molybdate and stannous chloride.

2. Enzymatic Method: Enzymatic assays utilize specific enzymes that catalyze the conversion of phosphate-containing compounds into products that can be measured. For example, the enzyme alkaline phosphatase can be used to hydrolyze phosphate esters, and the resulting reaction can be quantified using spectrophotometric methods.

3. Ion-Selective Electrode (ISE) Method: This method involves the use of ion-selective electrodes that directly measure the concentration of phosphate ions in the sample. The ISE method offers the advantage of rapid results and is often used for point-of-care testing.

4. Complexometric Titration: In this method, phosphate ions in the sample react with a known concentration of a metal cation, such as magnesium or calcium, in the presence of a complexing agent. The endpoint of the titration is detected using a color indicator or a potentiometric method, and the concentration of phosphate can be calculated based on the stoichiometry of the reaction.

5. High-Performance Liquid Chromatography (HPLC): HPLC can be used to separate and quantify phosphate compounds in complex biological samples such as blood. This method offers high sensitivity and specificity but requires specialized equipment and expertise.

Each method has its advantages and limitations, and the choice of method may vary depending on factors such as the required sensitivity, specificity, cost, and available resources. Regardless of the method used, accurate measurement of blood phosphate levels is essential for the diagnosis and management of various medical conditions, including disorders of calcium and phosphate metabolism, kidney disease, and metabolic bone disorders.

HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) METHOD

Using high-performance liquid chromatography (HPLC) to measure phosphate levels in blood involves several steps. Here's a stepwise procedure for measuring phosphate with the HPLC method:

1. Sample Preparation:

- Obtain the blood sample from the patient using standard venipuncture techniques.
- Centrifuge the blood sample to separate the plasma or serum from the cellular components. The plasma or serum is typically used for HPLC analysis.
- Transfer the plasma or serum to a clean, labeled tube for further processing.

2. Derivatization (Optional):

- If necessary, derivatize the phosphate compounds in the sample to improve their detectability by HPLC. Derivatization involves chemically modifying the phosphate molecules to form derivatives that are more suitable for chromatographic separation and detection.

3. Standard Preparation:

- Prepare a series of phosphate standard solutions with known concentrations to generate a calibration curve. These standards will be used to quantify the phosphate content in the sample.

4. Chromatographic System Setup:

- Set up the HPLC system according to the manufacturer's instructions.

- Choose an appropriate chromatographic column and mobile phase for the separation of phosphate compounds. Commonly used columns for phosphate analysis include ion-exchange and reverse-phase columns.

- Optimize the chromatographic conditions, including flow rate, temperature, and gradient elution program, if applicable.

5. Sample Injection:

- Inject a small volume of the prepared sample or derivatized sample into the chromatographic system using an autosampler or manual injection method.

6. Chromatographic Separation:

- Run the chromatographic method to separate the phosphate compounds present in the sample. Phosphate ions will elute from the column at different retention times based on their chemical properties.

7. Detection:

- Detect the eluted phosphate compounds using a suitable detector, such as a UV-Vis detector or a fluorescence detector. Phosphate derivatives may have specific absorbance or fluorescence properties that allow for sensitive detection.

8. Quantification:

- Quantify the amount of phosphate in the sample by comparing the peak area or peak height of the phosphate compounds in the sample chromatogram to the calibration curve generated from the standard solutions.

9. Data Analysis:

- Use software or data processing tools to analyze the chromatographic data and calculate the concentration of phosphate in the sample based on the calibration curve.

10. Quality Control:

- Perform quality control checks to ensure the accuracy and precision of the HPLC analysis. This may include running replicate samples, analyzing control samples with known concentrations, and monitoring system performance over time.

CHAPTER FOUR

RESULTS

Calcium

		calcium Control	First Trimester Calcium	Second trimester Calcium	Third Trimester calcium
Calcium Control	Pearson Correlation	1	-.948	-.866	.088
	Sig. (2-tailed)		.206	.333	.944
	N	3	3	3	3
First Trimester Calcium	Pearson Correlation	-.948	1	.574	.346
	Sig. (2-tailed)	.206		.106	.362
	N	3	9	9	9
Second trimester Calcium	Pearson Correlation	-.866	.574	1	.335
	Sig. (2-tailed)	.333	.106		.344
	N	3	9	10	10
Third Trimester calcium	Pearson Correlation	.088	.346	.335	1
	Sig. (2-tailed)	.944	.362	.344	
	N	3	9	10	11

Phosphate

		Phosphate Control	First Trimester phosphate	Second trimester phosphate	Third Trimester phosphate
Phosphate Control	Pearson Correlation	1	-.951	-.975	.731
	Sig. (2-tailed)		.201	.143	.478
	N	3	3	3	3
First Trimester phosphate	Pearson Correlation	-.951	1	.850**	-.245
	Sig. (2-tailed)	.201		.004	.525
	N	3	9	9	9
SECOND trimester phosphate	Pearson Correlation	-.975	.850**	1	.002
	Sig. (2-tailed)	.143	.004		.997
	N	3	9	10	10
Third Trimester phosphate	Pearson Correlation	.731	-.245	.002	1
	Sig. (2-tailed)	.478	.525	.997	
	N	3	9	10	11

Studies indicate that maternal serum calcium levels continue to increase during the third trimester to meet the rising fetal requirements (Hillman, 2000). This elevation is facilitated by enhanced absorption in the intestines and mobilization from maternal bone reserves, ensuring a sufficient supply for fetal skeletal mineralization and maternal physiological functions (Harvey *et al.*, 2009).

CHAPTER FIVE

5.0) DISCUSSION

Pregnancy represents a profound physiological journey characterized by substantial changes within the maternal body aimed at supporting fetal growth and ensuring a successful delivery. Amidst the numerous transformations that occur during pregnancy, the regulation of calcium and phosphate metabolism emerges as crucial for the well-being of both the mother and the developing fetus. This discourse aims to explore the intricate relationship between the progression of pregnancy and the dynamic equilibrium of calcium and phosphate, illuminating the physiological mechanisms at play and their implications for maternal and fetal health. Throughout pregnancy, maternal adaptations are orchestrated to meet the increasing requirements for calcium and phosphate, fundamental elements essential for the mineralization of fetal bones, dental development, and various cellular functions. The advancing stages of pregnancy instigate a series of hormonal fluctuations, prominently involving parathyroid hormone (PTH), calcitonin, and vitamin D, collectively responsible for maintaining the balance of calcium and phosphate within the body (Kovacs, 2005). Paramount in preserving calcium levels is PTH, synthesized by the parathyroid glands in response to diminishing serum calcium concentrations. With the progression of pregnancy, maternal PTH levels rise to ensure an ample supply of calcium for fetal bone formation, despite the physiological escalation in calcium demand. Additionally, the surge in estrogen during pregnancy amplifies the action of PTH, augmenting renal calcium reabsorption and bone turnover to meet the heightened requisites (Kovacs & Kronenberg, 1997).

Conversely, calcitonin, produced by the thyroid gland, counteracts the elevation in maternal calcium levels by inhibiting bone resorption and facilitating renal calcium excretion. Though the role of calcitonin in pregnancy is comparatively less understood than that of PTH, its significance in maintaining calcium homeostasis cannot be disregarded, particularly during the latter stages of gestation when calcium demands peak (Prentice, 2000).

Vitamin D, often dubbed as the sunshine vitamin, assumes a pivotal role in calcium and phosphate metabolism by promoting the intestinal absorption of these minerals. Throughout pregnancy, maternal vitamin D levels undergo fluctuations influenced by factors such as sunlight exposure, dietary intake, and supplementation. Deficiency in vitamin D during pregnancy not only jeopardizes maternal skeletal health but also compromises fetal bone mineralization, heightening the risk of adverse outcomes such as neonatal hypocalcemia and rickets (Kovacs, 2016). Moreover, the placenta serves as a crucial interface for the exchange of nutrients between the mother and the fetus, facilitating the transfer of calcium and phosphate to support fetal growth and development. Governed by various transporters and channels, placental transport mechanisms ensure a consistent supply of these minerals to the developing fetus, thereby influencing fetal bone formation and mineralization. The progressive growth of pregnancy exerts a significant strain on maternal calcium and phosphate reserves, necessitating adaptive responses to maintain the delicate balance essential for maternal and fetal well-being. Nonetheless, disruptions in calcium and phosphate metabolism, whether stemming from maternal dietary inadequacies, hormonal imbalances, or pathological conditions, can have profound implications for both maternal and fetal health.

5.1) CONCLUSION

The intricate interplay between the progression of pregnancy and calcium-phosphate metabolism underscores the complex physiological adaptations required to meet the escalating demands of fetal development. A comprehensive comprehension of these mechanisms is imperative for optimizing maternal nutritional status, mitigating the risk of adverse pregnancy outcomes, and safeguarding the long-term health of both mother and child.

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APPENDIX

CALCIUM

Case Summaries

				RESULT
TRIMESTER	control	1		5.70
		2		7.40
		3		5.10
		Total	Mean	6.0667
			Std. Deviation	1.19304
			Minimum	5.10
			Maximum	7.40
	1st trimester	1		6.80
		2		5.50
		3		6.70
		4		9.70
		5		5.30
		6		5.60
		7		5.80
		8		5.00
		9		4.50
		Total	Mean	6.1000
			Std. Deviation	1.53786
			Minimum	4.50
			Maximum	9.70
	2nd trimester	1		6.00
		2		4.90
		3		8.90
		4		7.10
		5		4.40
		6		4.10
		7		6.30
		8		5.30
		9		5.20
		10		4.40
		Total	Mean	5.6600
			Std. Deviation	1.47663
			Minimum	4.10
			Maximum	8.90
	3rd trimester	1		8.40
		2		6.40

		3		5.30
		4		5.90
		5		2.30
		6		4.60
		7		5.40
		8		3.50
		9		5.90
		10		4.50
		11		4.60
		Total	Mean	5.1636
			Std. Deviation	1.58762
			Minimum	2.30
			Maximum	8.40
	Total	Mean		5.6515
		Std. Deviation		1.49523
		Minimum		2.30
		Maximum		9.70

PHOSPHATE

Case Summaries

				RESULT
TRIMESTER	control	1		8.30
		2		8.30
		3		7.70
		Total	Mean	8.1000
			Std. Deviation	.34641
			Minimum	7.70
			Maximum	8.30
	1st trimester	1		10.40
		2		8.50
		3		14.50
		4		10.40
		5		9.70
		6		9.60
		7		9.30
		8		7.90
		9		9.60
		Total	Mean	9.9889
			Std. Deviation	1.87513
			Minimum	7.90

		Maximum	14.50
2nd trimester	1		12.30
	2		10.60
	3		17.90
	4		8.90
	5		11.20
	6		8.00
	7		10.10
	8		8.90
	9		8.80
	10		8.90
	Total	Mean	10.5600
		Std. Deviation	2.89528
		Minimum	8.00
		Maximum	17.90
3rd trimester	1		12.30
	2		9.50
	3		8.30
	4		8.60
	5		9.80
	6		10.70
	7		7.70
	8		9.90
	9		10.30
	10		5.50
	11		9.30
	Total	Mean	9.2636
		Std. Deviation	1.76311
		Minimum	5.50
		Maximum	12.30
Total	Mean		9.7485
	Std. Deviation		2.18477
	Minimum		5.50
	Maximum		17.90