IJPSR (2023), Volume 14, Issue 7 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 08 October 2022; received in revised form, 02 May 2023; accepted 30 May 2023; published 01 July 2023

EVALUATION OF SERUM VITAMIN D AND VARIOUS ORGANS FUNCTION TESTSIN DIFFERENT TRIMESTERS OF PREGNANCY: A SYSTEMATIC REVIEW

Satya Prakash *, Raj Kumar and Indra Prasad Adhikari

Department of Biochemistry, BRD Medical College, Gorakhpur - 273013, Uttar Pradesh, India.

Keywords:

Vitamin D, Pregnancy, Neonates, Calcium, Cholecalciferol (1, 25$(OH)_2$ D)

Correspondence to Author:
Dr. Indra Prasad Adhikari

Demonstrator,
Department of Biochemistry,
BRD Medical College, Gorakhpur - 273013, Uttar Pradesh, India.

E-mail: harshaladhikari@gmail.com

ABSTRACT: Background: Vitamin D is a lipid-soluble vitamin that plays an important role in maintaining calcium and phosphorus homeostasis and promoting bone metabolism. It sustains normal values of calcium and phosphorus in the systemic circulation. If the exogenous calcium sources are insufficient, vitamin D together with the parathyroid hormone (PTH) will direct part of the bone calcium. Circulating serum 1, 25$(OH)_2$ D gradually increases during the 1st and 2nd trimesters, owing to an increase in Vitamin D-binding protein concentrations in the maternal circulation. However, it is the free levels of 1, 25$(OH)_2$ D, which are actually responsible for enhancing transport of calcium across the placenta. Hormonal changes initiated even before conception significantly alter maternal biochemistry early in pregnancy. Steroid hormones, peptide hormones and prostaglandins interact to expand blood and plasma volume and modulate the maternal capacity to supply energy and nutrients to the fetoplacental unit.

INTRODUCTION: Vitamin D is a lipid-soluble vitamin that plays an important role in maintaining calcium and phosphorus homeostasis and promoting bone metabolism. In recent years, the role of vitamin D in the maintenance of extracellular health has drawn much attention. In terms of metabolism, during pregnancy, there is a good deal of research and controversy regarding the effects of vitamin D levels during pregnancy on foetal well-being and neonates [1, 2]. Recent evidences indicate a role of maternal diet during pregnancy on different birth outcomes such as length of gestation and fetal growth. An adequate intake of micronutrients in mothers, especially during pregnancy and lactation, is very important [3].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(7).3337-44

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.14(7).3337-44

Calcium and vitamin D is an essential nutrient and improves metabolic function, bone health and neuromuscular function [4]. It sustains normal values of calcium and phosphorus in the systemic circulation. If the exogenous calcium sources are insufficient, vitamin D together with the parathyroid hormone (PTH) will direct part of the bone calcium towards the general circulation in order to have balanced serum calcium values.

Serum 25(OH)D concentrations are often used as an indicator of vitamin D status, although 25(OH)D is present in serum in nanogram amounts and 1,25$(OH)_2$ D is present in pictogram amounts, long-term Vitamin D deficiency can result in increased PTH concentrations and decreased serum 1,25$(OH)_2$D concentrations, leading to osteomalacia [8]. Few randomized nutritional vitamin D interventions have been conducted during pregnancy and the importance of maternal vitamin D intake is best illustrated in observational studies of women with poor vitamin D status.

Although India is a tropical country with abundant sunshine; still Vitamin D deficiency is very common in India in all age groups and both sexes across the country [5]. Our aim is to provide a comprehensive picture of Vitamin D status among pregnant women [6].

Vitamin D Levels in Pregnancy: Mother is the sole source of vitamin D for her developing fetus during pregnancy than any time of the life cycle. Intestinal calcium absorption is only increased during the 3rd trimester [7]. Fetal calcium levels are higher than maternal throughout gestation. During the active pregnancy, vitamin D intake values tend to decrease from their optimal requirements for the body for several reasons such as body fat stores much of the vitamin D made in the skin it's less available to the body. This phenomenon may result in either vitamin D insufficiency or deficiency in the body, which in turn may affect the mother directly and later the offspring. There are specific risk factors that have the main influence to predispose vitamin D deficiency among pregnant women. The fetal skeleton begins to calcify in the last trimester, thereby increasing maternal demand for calcium.

This demand is met by increased production of 1,25(OH)2 D by the mother's kidneys and increased circulation of vitamin D through placenta to fetus. Circulating concentrations of 1, $25(OH)_2$ D gradually increase during the 1st and 2nd trimesters, owing to an increase in Vitamin D-binding protein concentrations in the maternal circulation. However, it is the free levels of 1, 25(OH) 2 D, which are responsible for enhancing transport of calcium across the placenta [8]. Fetal Vitamin D concentrations are up to 20% lower than maternal as measured in cord blood. In full-term infants, impaired fetal bone ossification is correlated with maternal Vitamin D deficiency. Maternal Vitamin D deficiency is associated with subtle fetal bone abnormalities like shorter knee-heel length, low birth weight and high risk of being small for gestational age [8].

Calcium Levels in Pregnancy: Calcium levels in blood affect many extracellular and intracellular processes. These include neural transmission, membrane stability, bone structure, blood coagulation, muscle movement and intracellular signalling. It is also an important cofactor for hormonal secretion in endocrine organs. There is an increasing evidence of lower than the recommended dietary allowance (RDA) of calcium intake in Indian population [9]. Inadequate dietary intake of calcium may lead to decrease in serum calcium level. Serum calcium level in human body is not only regulated by dietary calcium intake, but it is also influenced by many other factors like level of parathyroid hormones, vitamin D and exposure to sunlight [10]. During pregnancy, the absorption of calcium from the intestine is increased, correlating directly with maternal calcium intake. Calcium is actively transported to the fetus by the placenta. If calcium intake during pregnancy is low, calcium release from the maternal bones becomes prevalent towards the end of the pregnancy this may lead to low maternal bone mineral density (BMD), risk of delayed bone maturation of the new born and decreased BMD or teeth firmness of the off spring in later life [11]. Serum calcium level decreases during second and third trimester of pregnancy, primarily due to hemodilution [12]. Calcium requirement in non-pregnant state is 600 mg/day which increases to 1,200 mg/day during pregnancy [13].

This increased amount of calcium is required for the growth and development of bones and teeth of fetus. This demand can be met by the increased intake of calcium during pregnancy. Some complications of pregnancy may be associated with lower serum calcium level *e.g.* pre-eclampsia during pregnancy, low birth weight, preterm delivery and neonatal death [14]. Total serum calcium decreases gradually throughout pregnancy. This is associated with and parallels the drop in serum albumin (to which 60% of the serum calcium is attached) that results from expansion of the extracellular fluid volume. When adjustments are made for changes in serum albumin or protein concentration, little or no change in the total serum calcium level is apparent during pregnancy and serum ionic calcium changes are minimal [15].

First Trimester (Week 1 to 12): during the first trimester, the baby in utero develops from being a fertilised ovum to a fetus of about 6cm in length at 12 weeks. By the end of the first trimester, the developing fetus heart starts to beat. At the same

time the brain, stomach and the intestine also begins to develop at the end of first trimester [16].

Second Trimester (12 to 28 Weeks): Duringthe second trimester, pregnancy grows more and pregnant Women starts gaining weight gradually. For many people, this is the best part of pregnancy because the morning sickness and fatigue of their first trimester fades away slowly. Often, any sort of anxiety that was felt with the first trimester also starts to diminish at this point. Pregnant women start to feel fetus movements by the end of this trimester and you might begin to settle into your pregnancy and enjoy it more. Of course, it's important to remember that pregnancy is different for everyone. Some people never experience negative symptoms like morning sickness in their first trimester. Others might continue to feel sick well into their second trimester of pregnancy. Women might also feel or develop a few new symptoms of pregnancy during your second trimester,

Including:

1. An increased inappetite.
2. An achy body.
3. Some swelling in your hands, feet and ankles.
4. Some stretch marks [17].

Third Trimester (29 to 40th Week): At 32 weeks, the bones become soft and almost fully formed, late preterm births occur between 34 and 36 weeks [18]. Infants born at 39 or 40 weeks of pregnancy are considered full term. These infants have better health and outcomes than do infants born earlier or later than this period.

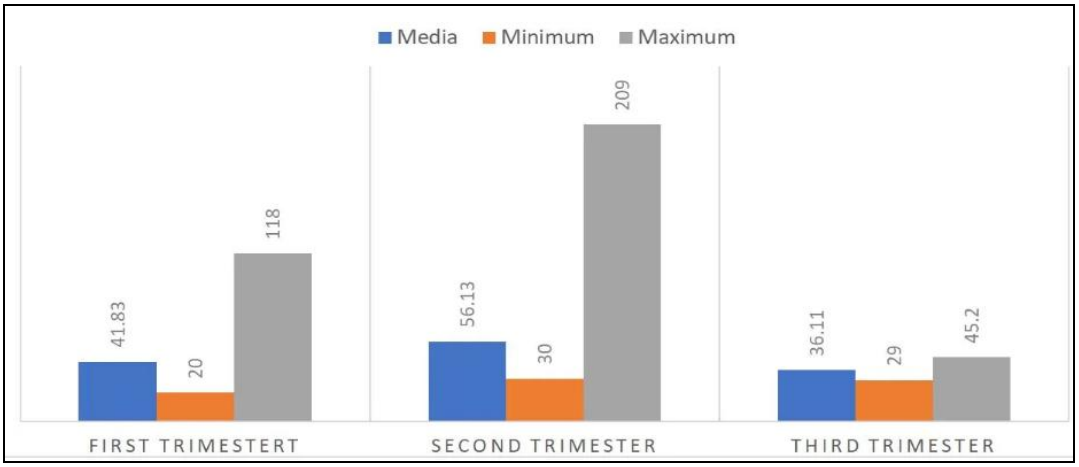

FIG. 1: AVERAGE LEVEL OF SERUM VITAMIN D INDIFFERENT TRIMESTERS OF PREGNANCY [ng/mL]

Biochemical Changes During Pregnancy: Major adaptations in maternal physiology and metabolism are required for successful pregnancy outcome. Hormonal changes initiated even before conception significantly alter maternal biochemistry early in pregnancy. Steroid hormones, peptide hormones, and prostaglandins interact to expand blood and plasma volume and modulate the maternal capacity to supply energy and nutrients to the fetoplacental unit [19].

Renal Function: Early in first trimester renal plasma flow and glomerular filtration rate each rise by approximately 60% above preconception values, resulting in a fall in serum creatinine, urea and urate by 25%. Measures of renal function then remain steady throughout pregnancy.

In the third trimester renal plasma flow declines to preconception values and serum creatinine trends upwards towards pre-pregnancy levels [20]. During pregnancy the serum sodium is about 3-5 mmol/L lower than normal because of an increase in intravascular volume and the resetting of the osmotic. Cardiac output and renal blood flow are also increased.

This leads to an increased glomerular filtration rate (GFR) with resultant decrease in concentrations of serum urea, creatinine and uric acid [21]. The renal tubular threshold is also lowered in pregnancy. This results in an increased excretion of uric acid, amino acids and glucose. Urinary testing for glycosuria can therefore be misleading. Similarly, urinary testing to assess metabolic changes should not be

used during pregnancy and is best delayed well into the post-partum period. The best practical uses of urine testing during pregnancy are to diagnose pregnancy itself, to detect asymptomatic bacteria and to warn for imminent pre-eclampsia when protein excretion rises [21]. Despite activation of the rennin-angiotensin-aldosterone system (RAAS) in early pregnancy, a simultaneous relative resistance to angiotensin II develops, counter balancing the vasoconstrictive effect and allowing profound vasodilatation [22].

This insensitivity to angiotensin II may be explained by the effects of progesterone and vascular endothelial growth factor mediated prostacyclin production, as well as modifications in the angiotensin I receptors during pregnancy [23]. The vascular refractoriness to angiotensin II may also be shared by other vasoconstrictors such as adrenergic agonists and arginine vasopressin (AVP) [24]. It is possible that in the second half of pregnancy, the placental vasodilators are more important in the maintenance of the vasodilator state [25].

Reduced Serum Osmolality: Another important change to salt and water handling in pregnancy is the re-setting of the osmotic balance. Osmolality can decrease early in pregnancy, usually as early as 6 weeks and can reach its lowest point at 10 weeks gestation [26]. The decrease in osmolality can be up to10mmol/kg and is because vasopressin is secreted at lower osmolality than in non-pregnant women [27].

Liver Enzymes: All markers of liver functions are generally reduced or are low during pregnancy due to the expansion of extracellular fluid. Hence pregnancy is associated with mild falls in serum albumin, alanine aminotransferase, aspartate aminotransferase (AST), gamma-glut amyl transferase (GGT) and total bilirubin are low compared with the non-pregnant state .The only exception is serum alkaline phosphatase (ALP) which is elevated due to ALP of placental origin. This may be related to lower intake of hepatotoxic drugs and alcohol in pregnancy [28]. Pregnancy is also associated with a fall in serum albumin beyond what would be expected from the increase in circulating volume, and despite a 50% increase in albumin synthesis in the liver, it has been hypothesized that there might be albumin catabolism to improve delivery of amino acids to the fetus [29]. Some authors have reported that lactate dehydrogenase (LDH) may rise from in first trimester, normal values in third trimester being up to double values pre-pregnancy. Other authors report no change in LDH. Levels of cholic acid and deoxycholic acid are unchanged during pregnancythough levels of chenodeoxycholic acid increase significantly postpartum [30].

Levels of alkaline phosphatase (ALP) rise due to production of the placental iso-enzyme, as well as a significant increase in bone iso-enzyme in third trimester. Prothrombin time falls progressively from the second trimester such that values are approximately 10–20% lower than preconception values in the third trimester [31]. This may be important when considering abnormal hepatic synthetic function with disorders such as amplified fragment length polymorphism. Serum amylase activity is similar in non-pregnant women and pregnant women in all trimesters of pregnancy. Serum lipase activity is significantly low in the first trimester but not in the later trimesters compared with non-pregnant women [32].

Cardiac Changes during Pregnancy: The cardiac output first increases by 20% till 8^{th} week of gestation, that further rises up to 40% and maximum increase is observed at $20\text{-}28^{th}$ week of gestation. There is further increase in cardiac output, stroke volume and heart rate. In the first two trimesters, blood pressure is lower than normal but it returns to normal in the third trimester. There is an increased risk of pulmonary oedema, if there is increased pulmonary capillary permeability secondary to pre-eclampsia. The cardiovascular changes are mediated by nitric oxide, estradiol and prosta-glandins [33].

Calcium Level during Pregnancy: Calcium metabolism in pregnancy is a complex process involving calcium, phosphorus, vitamin D, parathyroid hormone (PTH) and calcitonin (CT). Calcium absorption is enhanced in pregnancy and increased storage in the maternal skeleton probably occurs as well[34].During pregnancy, serum total calcium, phosphate and magnesium tend to be low due to the expanded intravascular space. Concentrations of calcium are also affected by the reduced albumin concentration.

However, results all remain within the reference range. If there is any doubt regarding the calcium result, measure the ionized calcium concentration as it remains unchanged during normal pregnancy despite changes in vascular volume and binding proteins. The concentration of serum parathyroid hormones tends to be 50% lower in pregnancy, despite the increased urinary excretion of calcium as a result of the increased GFR [35]. Although primary hyperparathyroidism is rare, it remains the commonest cause of hypercalcaemia during pregnancy. However, differentiating it biochemically from familial hypocalciuria, hypercalcaemia (which has non-surgical management) is difficult and evaluation at a specialist endocrinology clinic is recommended.

In contrast, the serum total and ionized calcium have been reported to fall during the last several days of pregnancy in the rate. Maternal losses of calcium to a litter of rapidly growing foetuses may exceed the maternal capacity to maintain a normal serum calcium level. Indeed, litter sizes correlated with lower serum calcium in pregnant state. In the pregnant women serum calcium falls in the last 1 to 2 weeks of gestation. Pregnant women have a mild decrease in total serum calcium over the last 6 weeks of pregnancy, likely due to the fall in serum albumin moreover, in one study, about 13% of pregnant women were found to develop signs and biochemical evidence of hypocalcaemia in the last month of pregnancy. Therefore, data from various study suggested that maternal blood calcium regulation may be disrupted by fetal demands in late pregnancy [36].

Correlation of Vitamin D3 with Pregnancy: variation and significance of Vitamin D metabolism during pregnancy and fetal development as compared to non-pregnant and no fetal development states, is a point that has been known for at least the past three decades but which has received little attention until recently [37]. The conversion of vitamin D to 25(OH)D appears unchanged during pregnancy, following first- and zero-order enzyme kinetics by contrast, the conversion of 25(OH)D to $1,25(OH)_2D$ during pregnancy is unique and unparalleled during life. At no other time during life is 25(OH)D so closely linked with $1,25(OH)_2D$. By 12 weeks of gestation, $1,25(OH)_2D$ levels are more than twice that of a non-pregnant adult and continue to rise two- to three fold from the non-pregnant baseline rising to over 700 pmol/l, attaining levels that would be toxic due to hypercalcaemia to the non-pregnant individual, but which are essential during pregnancy [38]. Recent evidences suggest that vitamin D deficiency is common during pregnancy especially among high-risk groups, including vegetarians, women with limited sun exposure (e.g., those who live in cold climates, reside in northern latitudes, or wear sun and winter protective clothing) and ethnic minorities, especially those with darker skin [39, 40]. New-born vitamin D levels are largely dependent on maternal vitamin D status.

Consequently, infants of mothers with or at high risk of vitamin D deficiency are also at risk of vitamin D deficiency. In 2010, the Food and Nutrition Board at the Institute of Medicine of the National Academies established that an adequate intake of vitamin D during pregnancy and lactation was 600 international units per day [41]. Most prenatal vitamins typically contain 400 international units of vitamin D per tablet. Summarizing recent observational and interventional studies, the authors of a recent clinical report from the Committee on Nutrition of the American Academy of Paediatrics suggested that a daily intake higher than that recommended by the Food and Nutrition Board may be needed to maintain maternal Vitamin D sufficiency [42].

Although data on the safety of higher doses are lacking, most experts agree that supplemental vitamin D is safe in dosages up to 4,000 international units per day during pregnancy or lactation [41]. They recommends an intake of 600 UL of vitamin D to pregnant women with the goal to achieve in serum more than 50 nmol/L (20 ng/mL) 25(OH)D considered by them as a sufficient level [43]. However, the US Endocrine Society suggests that at least 1,500–2,000 IU/of vitamin D may be needed to maintain blood levels of 25(OH)D above 75 nmol/L (30 mg/dL) and that should be considered the sufficient level for pregnant women . Nevertheless, both societies agree to consider the upper limit of intake as 4,000 IU/day [44]. Since evidence is lacking regarding appropriate cut-off points to define vitamin D status during pregnancy, levels used to establish intake recommendations

and vitamin D content of prenatal vitamin supplements are quite conservative. For pregnant women thought to be at increased risk of vitamin D deficiency, maternal serum 25-OH-D levels can be considered and should be interpreted in the context of the individual clinical circumstance. When vitamin D deficiency is identified during pregnancy, most experts agree that 1,000–2,000 international units per day of vitamin D is safe. Higher dose regimens used for the treatment of vitamin D deficiency have not been studied during pregnancy. Recommendations concerning routine vitamin D supplementation during pregnancy beyond that contained in a prenatal vitamin should await the completion of on-going randomized clinical trials. At this time, there is insufficient evidence to recommend vitamin D supplementation for the prevention of preterm birth or preeclampsia [45].

The circulating level of 25(OH)D during pregnancy is adequate to improve foetal development and prevent maternal complications. In fact, maternal and foetal health endpoint might even differ in the appropriate time for supplementation during pregnancy and required dose. Future studies should establish the exact 25(OH)D level that can be deemed sufficient for improved maternal and perinatal health owing to the lack of consensus in the literature. Adequate nutritional vitamin D status during pregnancy is important for fetal skeletal development, to the enamel formation, and perhaps general fetal growth and development. There also is mounting evidence to suggest that vitamin D deficiency impacts on the immune function, not only of the mother [46].

Future Perspective: We envision that over the next decade, the concept that vitamin D is actually a pre-prohormone and a potent mediator of the immune system will move from the perspective of heresy to one that is well-established. Such a paradigm shift will occur because of the mounting evidence that is being amassed to prove this point. What we know now is but a fraction of what we will learn in the decades to come. With improved understanding of vitamin D mechanisms of action come effective interventions. When any precursor to a hormone is restored and health characteristics improve, the overall disease burden diminishes. As such, there are several groups who will directly benefit from this paradigm shift women, most notable Asian, African-American and Hispanic women and their developing fetuses and lactating women and their recipient infants. This is what we expect will happen. Only the test of time may prove our hypothesis correct [38].

CONCLUSION: The results of this study showed that the mean vitamin D concentration in pregnant women and their neonates is low and there is a direct relationship between the levels of maternal vitamin D at delivery and neonatal cord blood vitamin D.

The present study highlights the need for a national guideline on vitamin D supplementation and treatment in pregnancy to reduce the risk of health problems in infancy. Maternal vitamin D reserves are dependent and vitamin D supplementation during pregnancy, that are likely to provide beneficial outcomes. However, recommendations regarding the intake of vitamin D supplementations need to be drawn.

Financial Support and Sponsorship: Nil.

ACKNOWLEDGMENTS: The authors did not receive any specific grant from any funding agency in the public, commercial, or non-profit sectors.

CONFLICT OF INTERESTS: Authors have no conflict of interests.

REFERENCE:

1. Salle BL, Delvin EE and Lapillonne A: Perinatal metabolism of vitamin D. Am J Clin Nutr 2000; 71: 1317-24.
2. Wagner CL, Taylor SN, Dawodu A, Johnson DD and Hollis BW: Vitamin D and its role during pregnancy in attaining optimal health of mother and fetus. Nutrients 2012; 4: 208–30.
3. Mohammad-Alizadeh-Charandabi S, Mirghafourvand M, Mansouri A, Najafi M & Khodabande F: The effect of vitamin d and calcium plus vitamin d during pregnancy on pregnancy and birth outcomes: a randomized controlled trial. Journal of Caring Sciences 2015; 4(1): 35–44. https://doi.org/10.5681/jcs.2015.004
4. Holick MF: Vitamin D: a D-Lightful health perspective. Nutrition Reviews 2008; 66(10): 182–94. https://doi.org/10.1111/j.1753-4887.2008.00104.x
5. American college of Obstetricians and gynecologist Committee on obstetric practice and society for Maternal-Fetal Medicine 2013.
6. Vitamin D Tests. Lab Tests Online (USA). American Association for Clinical Chemistry. Retrieved 2013.
7. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH and Weaver

CM: Endocrine Society. evaluation, treatment and prevention of vitamin d deficiency: an endo- crine society clinical practice guideline. Journal of Clinical Endocrinology & Metabolism 2011; 96: 1911-30. http://dx.doi.org/10.1210/jc.2011-0385
8. Barrett H and McElduff A: Vitamin D and Pregnancy: An Old Problem Revisited. Best Practice & Research Clinical Endocrinology & Metabolism 2010; 24; 527-39. http://dx.doi.org/10.1016/j.beem.2010.05.010
9. Kumar A, Meena M, Gyaneshwori Devi S, Gupta RK and Batra S: Calcium in midpregnancy. Arch Gynecol Obstet. 2009; 27:(3): 315-9.
10. Peacock M: Calcium metabolism in health and disease. Clin J Am Soc Nephrol 2010; 1: 23-30. http://dx.doi.org/10.2215/CJN.05910809 PMid
11. Kovacs C: Maternal mineral and bone metabolism during pregnancy, lactation and post-weaning recovery. Physiol Rev 2016; 96: 449–47
12. Pitkin RM and Gebhardt MP: Serum calcium concentrations in human pregnancy. Am J Obstet Gynecol 1977; 127(7): 775-8. http://dx.doi.org/10.1016/0002-9378(77)90256-3
13. Dietary Guidelines for Indians - a Manual. National Institute of Nutrition, India Council of Medical Research. NIN Press, Hyderabad 2011.
14. Sabour H, Hossein-Nezhad A, Maghbooli Z, Madani F, Mir E and Larijani B: Relationship between pregnancy outcomes and maternal vitamin D and calcium intake: A cross-sectional study. Gynecol Endocrinol 2006; 22(10): 585-9. 10.1080/09513590601005409 PMid
15. Pitkin RM: Calcium metabolism in pregnancy and the perinatal period: a review. Am J Obstet Gynecol 1985; 151: 99–09
16. Firsttrimester.pregnancybirth&baby.https://www.pregnancybirthbaby.org.au/first- trimester accessed on 15 September 2022
17. Pregnancy: Second Trimester. cleveland clinic https://my.clevelandclinic.org/health/articles/16092-pregnancy-second-trimester accessed on 15 September 2022
18. Matsuoka LY, Wortsman J, Haddad JG and Hollis BW: Skin types and epidermal photosynthesis of vitamin D3. J Am Acad Dermatol 1990; 23(3): 525–26.
19. Lockitch G: Clinical biochemistry of pregnancy. Crit Rev Clin Lab Sci 1997; 34(1): 67-39. doi: 10.3109/10408369709038216. PMID: 9055057
20. Cheung KL and Lafayette RA: Renal physiology of pregnancy. Adv Chronic Kidney Dis 2013; 20: 209–14
21. Tran HA: Biochemical tests in pregnancy. Aust Prescr 2005; 28: 136-9.
22. Gant NF, Worley RJ, Everett RB and MacDonald PC: Control of vascular responsiveness during human pregnancy. Kidney Int 1980; 18(2): 253–58.
23. Irani RA and Xia Y: Renin angiotensin signaling in normal pregnancy and preeclampsia. Semin Nephrol 2011; 31(1): 47–58
24. Conrad KP and Davison JM: The renal circulation in normal pregnancy and preeclampsia: is there a place for relaxin. Am J Physiol Renal Physiol 2014; 306(10): 1121–35
25. Tkachenko O, Shchekochikhin D and Schrier RW: Hormones and hemodynamics in pregnancy. Int J Endocrinol Metab 2014; 12(2): 14098. doi:10.5812/ijem.14098
26. Brown MA and Whitworth JA: The kidney in hypertensive pregnancies--victim and villain. Am J Kidney Dis 1992; 20(5): 427-42.
27. Akbari A, Wilkes P, Lindheimer M, Lepage N and Filler G: Reference intervals for anion gap and strong ion difference in pregnancy: a pilot study. Hypertens Pregnancy 2007; 26(1): 111-19.
28. Cattozzo G, Calonaci A and Albeni C: Reference values for alanine aminotransferase, alpha-amylase, aspartate aminotransferase, gamma-glutamyltransferase and lactate dehydrogenase measured according to the IFCC standardization during uncomplicated pregnancy. Clin Chem Lab Med 2013; 51: 239–41
29. Klajnbard A, Szecsi PB and Colov NP: Laboratory reference intervals during pregnancy, delivery and the early postpartum period. Clin Chem Lab Med 2010; 48: 237–48.
30. Lee RH, Ouzounian JG and Goodwin TM: Bile acid concentration reference ranges in a pregnant Latina population. Am J Perinatol 2013; 30: 389–93.
31. Gong JM, Shen Y and He YX: Reference intervals of routine coagulation assays during the pregnancy and puerperium period. J Clin Lab Anal 2016; 30: 912–17.
32. Karsenti D, Bacq Y and Brechot JF: Serum amylase and lipase activities in normal pregnancy: a prospective case-control study. Am J Gastroenterol 2001; 96: 697–99.
33. Sibai B, Dekker G and Kupferminc M: Pre-eclampsia. Lancet 2005; 365: 785-99.
34. Pitkin RM: Calcium metabolism in pregnancy: a review. Am J Obstet Gynecol 1975; 121(5): 724-37. doi: 10.1016/0002-9378(75)90481-0. PMID: 1090175
35. Seely EW, Brown EM, DeMaggio DM, Weldon DK and Graves SW: A prospective study of calciotropic hormones in pregnancy and post partum: reciprocal changes in serum intact parathyroid hormone and 1,25-dihydroxyvitamin D. Am J Obstet Gynecol 1997; 176: 214-7
36. Christopher S. Kovacs: Calcium and Bone Metabolism in Pregnancy and Lactation. The Journal of Clinical Endocrinology & Metabolism 2001; 86(6): 2344–48.https://doi.org/10.1210/jcem.86.6.7575
37. Bikle DD, Gee E, Halloran B and Haddad JG: Free 1,25-dihydroxyvitamin D levels in serum from normal subjects, pregnant subjects, and subjects with liver disease. J Clin Invest 1984; 74(6): 1966–71
38. Wagner CL, Taylor SN, Johnson DD and Hollis BW: The role of vitamin D in pregnancy and lactation: emerging concepts. Womens Health (Lond) 2012; 8(3): 323-40. doi: 10.2217/whe.12.17. PMID: 22554179; PMCID: PMC4365424.
39. Hollis BW and Wagner CL: Assessment of dietary vitamin D requirements during pregnancy and lactation. Am J Clin Nutr 2004; 79: 717–26.
40. Lee JM, Smith JR, Philipp BL, Chen TC, Mathieu J and Holick MF: Vitamin D deficiency in a healthy group of mothers and newborn infants. Clin Pediatr (Phila) 2007; 46: 42–4.
41. Institute of Medicine of the National Academies (US). Dietary reference intakes for calcium and vitamin D. Washington, DC: National Academy Press 2010.
42. Wagner CL and Greer FR: Prevention of rickets and vitamin D deficiency in infants, children and adolescents. American Academy of Pediatrics Section on Breastfeeding; American Academy of Pediatrics Committee on Nutrition. Pediatrics 2008; 122: 1142–52.
43. Ross AC, Taylor CL and Yaktine AL: Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. Washington (DC): National Academies Press (US); 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK56070/ doi: 10.17226/13050

44. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH and Weaver CM: Endocrine Society: Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. The Journal of Clinical Endocrinology and Metabolism 2011; 96: 1911–30.
45. Vitamin D: screening and supplementation during pregnancy. Committee Opinion No. 495. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011; 118: 197–8.
46. Hollis BW, Johnson D, Hulsey TC, Ebeling M and Wagner CL: Vitamin D supplementation during pregnancy: double-blind, randomized clinical trial of safety and effectiveness. The Journal of Bone and Mineral Research 2011; 26(10): 2341–57.

How to cite this article:
Prakash S, Kumar R and Adhikari IP: Evaluation of serum Vitamin D and various organs function testsin different trimesters of pregnancy: a systematic review. Int J Pharm Sci & Res 2023; 14(7):3337-44. doi: 10.13040/IJPSR.0975-8232.14(7).3337-44.