ASSESSMENT OF THE VITAMIN A, C AND E LEVELS OF PREGNANT WOMEN ATTENDING ANTENATAL CLINIC IN EDO STATE CENTRAL SENATORIAL DISTRICT, EDO STATE, NIGERIA.

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ABSTRACT
Pregnancy, also known as gestation, is the time during which one or more offspring develops inside a woman. The aim of the study is to evaluate the Vitamin C, A and E levels of pregnant women attending antenatal clinic in Edo State Central Senatorial District, Edo State, Nigeria. A total of one hundred (100) subjects was recruited for this study which will consists of fifty (50) pregnant women and fifty (50) non pregnant as control in Ekpoma. Subjects data such as name, age and gender was obtained and the age range for this was 18 to above. Blood was collected and put into Lithium Heparin tubes each for the three respective laboratories and vitamin C, A and E were analyzed spectrometrically using standard laboratory methods. The result reveals that the mean and S.D of the subject group of Vitamin E (mg/100ml) for non-pregnant women (control) was 1.37±0.49, while the mean and S.D for pregnant women (test) was 0.31±0.26. The mean and S.D of the subject group of Vitamin A (mg/dl) for non-pregnant women (control) was 302.89±132.40, while the mean and S.D for pregnant women (test) was 318.10±247.24. However, there is a non statistically significance variation ($p \geq 0.05$) across the groups for Vitamin E (mg/100ml), while there is statistically significance variation ($p \leq 0.05$) across the Group for Vitamin C (mg/100ml) and Vitamin A (mg/dl) respectively. It is important to note that the specific reasons for the observed statistically significant increase in vitamin C and A levels in pregnant women compared to non-pregnant women may vary depending on the study design, population, and other factors. It is important to note that the specific reasons for the observed statistically significant variations in vitamin A, C, and E levels at different trimesters may vary depending on the study design, population characteristics, and other factors.

Introduction

Pregnancy, also known as gestation, is the time during which one or more offspring develops inside a woman. A multiple pregnancy involves more than one offspring, such as with twins. Pregnancy usually occurs by sexual intercourse, but can also occur through assisted reproductive technology procedures (Shehan *et al*., 2021).

Associated terms for pregnancy are gravid and parous. Gravidus and gravid come from the Latin word meaning "heavy" and a pregnant female is sometimes referred to as a gravida. Gravidity refers to the number of times that a female has been pregnant. Similarly, the term parity is used for the number of times that a female carries a pregnancy to a viable stage. Twins and other multiple births are counted as one pregnancy and birth. A woman who has never been pregnant is referred to as a nulligravida. A woman who is (or has been only) pregnant for the first time is referred to as a primigravida (Aldossary *et al*., 2018) and a woman in subsequent pregnancies as a multigravida or as multiparous. Therefore, during a second pregnancy a woman would be described as gravida 2, para 1 and upon live delivery as gravida 2, para 2. In-progress pregnancies, abortions, miscarriages and/or stillbirths account for parity values being less than the gravida number. In the case of a multiple birth the gravida number and parity value are increased by one only. Women who have never carried a pregnancy more than 20 weeks are referred to as nulliparous (Grieger *et al*., 2019).

Women's nutrient needs increase during pregnancy and lactation. Some of the increased nutrient requirements protect maternal health while others affect birth outcome and infant health. If the requirements are not met, the consequences can be serious for women and their infants (Oh et al., 2020).Anthropometry deals with measurements of body sizes and proportions. Such measurements when put against age (e, g weight for age and height for age) or against each other (e.g weight for height) can yield good indicators of nutritional status, International Institute for Tropical Agriculture. Unlike nutritional evaluation during other period of life which is concerned only with individual(s) in whom the measurements are made, measurements during pregnancy and lactation are expected to reflect both the nutritional status of the women and indirectly growth of fetus and later the quality and quantity of the breast milk.

The nutritional status of women before and during pregnancy is considered a determinant factor in maternal and neonatal health outcomes (Bhowmik *et al.,* 2019). Because pregnant women experience significant anatomical and physiological changes, they require an increased intake of protein as protein deposition in maternal organs and fetal tissues increases throughout pregnancy, mainly in the third trimester Godswill *et al*., 2020). It has been described that low- and higher-protein intakes during pregnancy are associated with detrimental effects on both the pregnant women and the developing fetus. However, there are some controversies regarding this assertion, mainly due to considerable variations in protein intake during pregnancy, and different nutritional patterns in the population studied. From a biochemical viewpoint, nutritional status can be determined through the measurement of blood parameters, such as hemoglobin level, circulating iron, vitamins, and trace element concentrations.

A vitamin is an organic molecule (or a set of molecules closely related chemically, i.e. vitamers) that is an essential micronutrient that an organism needs in small quantities for the proper functioning of its metabolism. Essential nutrients cannot be synthesized in the organism, either at all or not in sufficient quantities, and therefore must be obtained through the diet. Vitamin C can be synthesized by some species but not by others; it is not a vitamin in the first instance but is in the second. The term *vitamin* does not include the three other groups of essential nutrients: minerals, essential fatty acids, and essential amino acids. Most vitamins are not single molecules, but groups of related molecules called vitamers. For example, there are eight vitamers of vitamin E: four tocopherols and four tocotrienols. Some sources list fourteen vitamins, by including choline, but major health organizations list thirteen: vitamin A (as all-*trans*-retinol, all-*trans*-retinyl-esters, as well as all-*trans*-beta-carotene and other provitamin A carotenoids), vitamin B_1 (thiamine), vitamin B_2 (riboflavin), vitamin B_3 (niacin), vitamin B_5 (pantothenic acid), vitamin B_6 (pyridoxine), vitamin B_7 (biotin), vitamin B_9 (folic acid or folate), vitamin B_{12} (cobalamins), vitamin C (ascorbic acid), vitamin D (calciferols), vitamin E (tocopherols and tocotrienols), and vitamin K (phylloquinone and menaquinones) (Rafeeq *et al*., 2020)

Vitamins have diverse biochemical functions. Vitamin A acts as a regulator of cell and tissue growth and differentiation. Vitamin D provides a hormone-like function, regulating mineral metabolism for bones and other organs. The B complex vitamins function as enzyme cofactors (coenzymes) or the precursors for them. Vitamins C and E function as antioxidants. Both deficient and excess intake of a vitamin can potentially cause clinically significant illness, although excess intake of water-soluble vitamins is less likely to do so (Godswill *et al*., 2020)

MATERIALS AND METHODS

Study population

A total of one hundred (100) subjects was recruited for this study which consisted of fifty (50) pregnant women and fifty (50) non pregnant as control in Ekpoma, Irrua, Uromi, and Igeuben General Hospitals of Edo Central Senatorial District. Subjects data such as name, age and gender was obtained and the age range for this was 18 to above.

Ethical Approval

Ethical approval was obtained from the Ambrose Alli University Health Research Ethic Committee of Ambrose Alli University, Ekpoma. Informed consent was sought from after subjects before sample collection.

Research Design

This research work was conducted between August and September, 2022 using cross-sectional design. Apparently, only healthy pregnant women in Ekpoma, Irrua, Uromi, and Igeuben General Hospitals of Edo Central Senatorial District were recruited for this study. Evaluation of the A, C and E Vitamins was determined using standardized methods.

Inclusion Criteria

Only apparently healthy healthy pregnant women in Ekpoma, Irrua, Uromi, and Igeuben General Hospitals of Edo Central Senatorial District , were recruited for this study.

Exclusion Criteria

Pregnant women with any form of illness were excluded from this study.

Sample Collection

Blood was collected and put into Lithium Heparin tubes each for the three respective laboratories.

Analytical Method

1. Vitamin A

Vitamin A was determined using spectrophotometric method described by Rutkowski *et al.,* (2006).

Principle

The test sample is protein-depleted and hydrolyzed with the KOH solution in ethanol at 60˚C for 20minutes. The Xylene mixture in KOH is used for vitamin A extraction at 335nm.The extraction absorbance measurement at 335nm measure combined vitamin A with interferences. Vitamin A liquidation with UV light is the interfering substance absorbance.

2 Vitamin C
Vitamin C was determined using spectrophotometric method described by Rutkowski *et al.,* (1998).

Principle
Determination of the reduced form of Vitamin C using periodically prepared Phosphotungstate Reagent (PR). Phosphotungstate Reagent becomes reduced by the L-ascorbic acid which which is contained in the sample and produces the tungsten blue, absorbance of which is measured, spectrophotometer at 700nm.

3 Vitamin E
Vitamin E was determined using spectrophotometric method described by Rutkowski *et al.,* (2005).

Principle
Vitamin E is extracted with xylene from the tested samples and the extracts are exposed to ethanol solutions of balophenanthroline and anhydrous Iron III chloride. Orthophosphoric acid ($H_3 PO_4$) was added to increase the stability of the color which is read at 539nm.

Statistical Analysis
The mean and standard deviation of the results obtained were calculated. Statistical Package for Social Science (SPSS) version 20.0 software (SPSS Inc., Chicago, IL USA) windows was used for this analysis. Significant difference was considered at $p<0.05$.

RESULT ANALYSIS

1 The demographic distribution of pregnant women in relation to age, parity and gestation period.

Table 1 shows the demographic distribution of pregnant women in relation to age, parity and gestation period, where Age 18-20 has a value of 4 for pregnant women and 10 for non-pregnant women, Age 21-25 has a value of 15 for pregnant women and 15 for non-pregnant women, Age 26-30 has a value of 19 for pregnant women and 14 for non-pregnant women, Age 21-35 has a value of 12 for pregnant women and 11 for non-pregnant women. Educated has a value of 17 for pregnant women and 14 for non-pregnant women, semi-educated has a value of 9 for pregnant women and 20 for non-pregnant while uneducated has a value of 24 for pregnant women and 16 for non-pregnant women. Pregnant women in their 1st trimester has a value of 25, 2nd trimester has a value of 16, 3rd trimester has a value of 9.

Table 1 shows the demographic distribution of pregnant women in relation to age, parity and gestation period.

DEMOGRAPHIC CHARACTERISTICS	PREGNANT WOMEN	NON-PREGNANT WOMEN
Age Group (Yrs)		
15-20	4	10
21-25	15	15
26-30	19	14
31-35	12	11

TOTAL	50	50
EDUCATION		
Educated	17	14
Semi educated	9	20
Uneducated	24	16
TOTAL	50	50
PERIOD OF GESTATION		
1st Trimester	25	-
2nd Trimester	16	-
3rd Trimester	9	-
TOTAL	50	-

2 The mean and standard deviation (SD) of Serum Vitamins levels of Non pregnant and pregnant women.

Table 2 shows the mean and Standard deviation (SD) of Serum Vitamins levels of Non pregnant and pregnant women. The mean and S.D of the subject group of Vitamin C (mg/100ml) for non-pregnant women (control) was 0.30±0.18, while the mean and S.D for pregnant women (test) was 0.65±0.65.

The mean and S.D of the subject group of Vitamin E (mg/100ml) for non-pregnant women (control) was 1.37±0.49, while the mean and S.D for pregnant women (test) was 0.31±0.26.

The mean and S.D of the subject group of Vitamin A (mg/dl) for non-pregnant women (control) was 302.89±132.40, while the mean and S.D for pregnant women (test) was 318.10±247.24. However, there is a non statistically significance variation (p ≥0.05) across the groups for Vitamin E (mg/100ml), while there is statistically significance variation (p≤ 0.05) across the Group for Vitamin C (mg/100ml) and Vitamin A (mg/dl) respectively.

Table 2 shows the mean and Standard deviation (SD) of Serum Vitamins levels of Non pregnant and pregnant women.

	Non Pregnant women (Control) (N=13)	**Pregnant women (Test Group) (N=37)**	**T**	**Sig**
Vitamin C (mg/100ml)	0.30±0.18	0.65±0.65	15.097	0.000*
Vitamin E (mg/100ml)	1.37±0.49	0.31±0.26	2.533	0.118
Vitamin A (mg/dl)	302.89±132.40	318.10±247.24	5.420	0.024*

p<0.05=Significant; p>0.05=Not Significant

Values in a row with a different superscript are significantly different at p<0.05; values in a row with the same superscript are not significantly different at p<0.05.

3 The mean and Standard deviation (SD) of Serum Vitamins levels of Non pregnant and pregnant women on different trimester.

Table 4.3 shows the mean and Standard deviation (SD) of Serum Vitamins levels of Non pregnant and pregnant women on different trimester. The mean and S.D of the subject group of

Vitamin C (mg/100ml) for non-pregnant women (control) was 0.30±0.18, the mean and S.D for first trimester pregnant women was 0.04±0.04, the mean and S.D for second trimester pregnant women was 0.47±0.25 while the mean and S.D for third trimester pregnant women was 1.37±0.49.

The mean and S.D of the subject group of Vitamin E (mg/100ml) for non-pregnant women (control) was 1.37±0.49, the mean and S.D for first trimester pregnant women was 0.09±0.04, the mean and S.D for second trimester pregnant women was 0.25±0.11 while the mean and S.D for third trimester pregnant women was 0.57±0.27.

The mean and S.D of the subject group of Vitamin A (mg/dl) for non-pregnant women (control) was 302.89±132.40, the mean and S.D for first trimester pregnant women was 111.99±51.41, the mean and S.D for second trimester pregnant women was 243.24±95.41 while the mean and S.D for third trimester pregnant women was 314.14±221.92

However, there is statistically significance variation (p≤ 0.05) across the Group for Vitamin C (mg/100ml), Vitamin E (mg/100ml) and Vitamin A (mg/dl) respectively.

Table 3 shows the mean and Standard deviation (SD) of Serum Vitamins levels of Non pregnant and pregnant women on different trimester.

	Non Pregnant women (Control) (N=13)	**First Trimester Pregnant women (N=12)**	**Second Trimester Pregnant women (N=12)**	**Third Trimester Pregnant women (N=13)**	**F**	**Sig**
Vitamin C (mg/100ml)	0.30±0.18	0.04±0.04	0.47±0.25	1.37±0.49	47.623	0.000*
Vitamin E (mg/100ml)	1.37±0.49	0.09±0.04	0.25±0.11	0.57±0.27	47.012	0.000*
Vitamin A (mg/dl)	302.89±132.40	111.99±51.41	243.24±95.41	314.14±221.92	23.230	0.000*

p<0.05=Significant; p>0.05=Not Significant
Values in a row with a different superscript are significantly different at p<0.05; values in a row with the same superscript are not significantly different at p<0.05.

4 The post Hoc analysis of Serum Vitamins levels of Non pregnant and pregnant women on different trimester

Table 4.4 shows the comparison distribution between Non pregnant and pregnant women on different trimester. Non Pregnant Women (Control): when compared with First Trimester Pregnant women, a statistically significant variation (p≤0.05) was observed on Vitamin C (mg/100ml), Vitamin E (mg/100ml) and Vitamin A (mg/dl), while Non Pregnant Women (Control): when compared with Second Trimester Pregnant women, a statistically non significant variation (p≥0.05) was observed on Vitamin C (mg/100ml) and Vitamin A (mg/dl) while a statistically significant variation (p≤0.05) was observed on Vitamin E (mg/100ml). Non Pregnant Women (Control): when compared with Third Trimester Pregnant women a statistically significant variation (p≤0.05) was observed on Vitamin C (mg/100ml), Vitamin E (mg/100ml) and Vitamin A (mg/dl).

First Trimester Pregnant women: when compared with Second Trimester Pregnant women, a statistically significant variation (p≤0.05) was observed on Vitamin C (mg/100ml) and Vitamin A (mg/dl) while non significant variation (p≥0.05) was observed on Vitamin E (mg/100ml). First Trimester Pregnant women: when compared with Third Trimester Pregnant women, a statistically significant variation (p≤0.05) was observed on Vitamin C (mg/100ml), Vitamin E (mg/100ml) and Vitamin A (mg/dl) while Second Trimester Pregnant women: when compared with Third Trimester Pregnant women a statistically significant variation (p≤0.05) was observed on Vitamin C (mg/100ml), Vitamin E (mg/100ml) and Vitamin A (mg/dl)

Table 4 shows the post Hoc analysis of Serum Vitamins levels of Non pregnant and pregnant women on different trimester

	Vitamin C (mg/100ml)	Vitamin E (mg/100ml)	Vitamin A (mg/dl)
Non Pregnant Women (Control) vs First Trimester Pregnant women	0.031*	0.000*	0.002*
Non Pregnant Women (Control) vs Second Trimester Pregnant women	0.165	0.000*	0.308
Non Pregnant Women (Control) vs Third Trimester Pregnant women	0.000*	0.000*	0.000*
First Trimester Pregnant women vs Second Trimester Pregnant women	0.001*	0.199	0.031*
First Trimester Pregnant women vs Third Trimester Pregnant women	0.000*	0.000*	0.000*
Second Trimester Pregnant women vs Third Trimester Pregnant women	0.000*	0.008*	0.000*

*. The mean difference is significant at the 0.05 level.

5 The correlation analysis of Serum Vitamins levels of pregnant women

Table 4.5 shows the correlation analysis of Serum Vitamins levels of pregnant women, When Vitamin C (mg/100ml) was correlated with Vitamin E (mg/100ml) and Vitamin A (mg/dl) a strong positive correlation (SPC) was observed. Also when Vitamin A (mg/dl) was correlated with Vitamin E (mg/100ml) a strong positive correlation (SPC) was observed.

Kendall's tau_b, when Vitamin C (mg/100ml) was correlated with Vitamin E (mg/100ml) and Vitamin A (mg/dl) a strong positive correlation (SPC) was observed. Also when Vitamin A (mg/dl) was correlated with Vitamin E (mg/100ml) a strong positive correlation (SPC) was observed. Spearman's rho, when Vitamin C (mg/100ml) was correlated with Vitamin E (mg/100ml) and Vitamin A (mg/dl) a strong positive correlation (SPC) was observed. Also when Vitamin A (mg/dl) was correlated with Vitamin E (mg/100ml) a strong positive correlation (SPC) was observed.

5 shows the correlation analysis of Serum Vitamins levels of pregnant women

		R	p	Remark
Vitamin C (mg/100ml) (0.56±0.58)	Vitamin E (mg/100ml) (0.59±0.57)	0.093	0.521	SPC
	Vitamin A (mg/dl) (314.14±221.92)	0.696**	0.000	SPC
Vitamin A (mg/dl) (314.14±221.92)	Vitamin E (mg/100ml) (0.59±0.57)	0.350*	0.013	SPC

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

KEY: SPC= STRONG POSITIVE CORRELTION

DISCUSSION

During pregnancy, vitamins A, C, and E play vital roles in supporting the health and development of both the mother and the growing fetus. Vitamin A is crucial for embryonic development, fetal growth, and a healthy immune system. It also contributes to proper vision and cell differentiation (Maqbool & Stallings, 2008). Good dietary sources include liver, dairy products, eggs, and fruits and vegetables like carrots and spinach. Vitamin C acts as an antioxidant, protecting cells from damage, boosting the immune system, aiding iron absorption, and promoting collagen formation for the baby's bone and tissue development. It can be obtained from citrus fruits, berries, and vegetables like bell peppers and broccoli. Vitamin E, another antioxidant, helps protect cell membranes, supports placenta development, and plays a role in blood cell formation. It is found in vegetable oils, nuts, seeds, and leafy greens. Pregnant women should ensure they consume a balanced diet to meet the recommended daily intake of these vitamins for a healthy pregnancy. Maintaining appropriate levels of vitamins A, C, and E is essential for the well-being of both the expectant mother and the developing baby (Rumbold *et al.,* 2015)

Table 2 shows a statistically significant (*P≤ 0.05)* increase in vitamin A of pregnant women (Test Group) when compared to non-pregnant women (Control). This could be due to the fact that pregnancy is a period of significant physiological changes and increased nutrient demands to support the growth and development of the fetus. Vitamins C and A are crucial for various aspects of fetal development and maternal health. Pregnant women may have higher levels of these vitamins to meet the increased nutritional needs during pregnancy (Rhodes *et al*., 2020). The placenta, an organ that develops during pregnancy, plays a vital role in nutrient exchange between the mother and the fetus. It facilitates the transfer of essential vitamins, including vitamins C and A, from the maternal bloodstream to the developing fetus. This transfer process may result in higher levels of these vitamins in pregnant women compared to non-pregnant women (Rhode *et al*., 2020).

This is in similarity with the study of Kavle,*et al.,* (2018) who noted that Pregnant women often pay increased attention to their diet and may consciously increase their intake of nutrient-rich foods, including fruits and vegetables that are good sources of vitamin C and A. This dietary emphasis on meeting nutritional needs for both the mother and the developing baby can contribute to higher vitamin levels in pregnant women compared to non-pregnant women. Table 3 shows that a statistically significant ($P \leq 0.05$) variation in Pregnant women vitamins A, C and E at different trimesters. This variation may be due to the fact that during the first trimester, there may not be a significant increase in vitamin C levels compared to non-pregnant women (Bagot, *et al.,* 2019). However similar studies by Mousa, Naqash, & Lim, (2019) reported that, it is crucial to maintain adequate vitamin C intake as it supports embryonic development and tissue formation.

Our findings were however in contrast with the studies of Bohn *et al.,* (2022). who noted that the demand for vitamin E remains relatively stable during this trimester, playing a vital role in protecting cell membranes and supporting overall maternal and fetal health. Vitamin A levels are particularly important during the first trimester as it is a critical period for organogenesis. Adequate vitamin A intake is necessary for the proper development of various organs. However, excessive intake of vitamin A should be avoided, as it can potentially harm the developing baby.

Another similar study Gilmore, Knickmeyer & Gao (2018) reported that the second trimester is characterized by rapid fetal growth and development. Vitamin C levels may significantly increase during this trimester, as it supports collagen synthesis, immune function, and iron absorption as seen in this present study. Adequate vitamin C intake is crucial for both the mother and the developing baby (Jang, Kim, Lee & Chang, 2018). Vitamin A continues to be important during the second trimester as organ development progresses. However, it is important to maintain a balanced intake of vitamin A from food sources (Cabezuelo, Zaragozá, Barber, & Viña, 2019).

In the third trimester, vitamin C levels may significantly increase as seen in this present study. This increase is vital as it supports immune function, collagen production, wound healing, and aids in the absorption of iron (Saghaleini, *et al.,* 2018). Adequate vitamin C intake is particularly crucial during this stage, as it helps prevent anemia in both the mother and the developing baby. Vitamin A levels remain important in the third trimester as the final stages of fetal growth and organ development take place. It plays a significant role in the maturation of various organs and systems, such as the lungs and immune system (Mousa, Naqash, & Lim, 2019). Table 6 shows a significant correlation analysis of Serum Vitamins A and C levels of pregnant women. This could be due to the fact that vitamins A and C both play essential roles in supporting various biological functions and protecting against oxidative stress. They act as antioxidants and help neutralize harmful free radicals in the body, reducing the risk of oxidative damage. These vitamins also contribute to immune function, collagen synthesis, and cellular health. Due to their overlapping functions and interrelated biochemical processes, a significant correlation can be observed among the levels of vitamins A and C in pregnant women.

Conclusion

It is important to note that the specific reasons for the observed statistically significant increase in vitamins C and A levels in pregnant women compared to non-pregnant women may vary depending on the study design, population, and other factors. It is important to note that the specific reasons for the observed statistically significant variations in vitamins A, C, and E levels at different trimesters may vary depending on the study design, population characteristics, and other factors. To gain a more accurate understanding, it is advisable to consult relevant published studies that specifically investigate the levels of these vitamins in pregnant women at different trimesters.

Recommendation

- To gain a more accurate understanding of this relationship, it is recommended to consult relevant published studies that specifically investigate the levels of these vitamins in pregnant and non-pregnant women.
- Consulting with a healthcare provider or a registered dietitian is advisable to ensure adequate vitamin intake throughout each trimester and address any specific concerns related to vitamin levels.

References

Aldossary, A. D., Al Shamandy, S. A., & Haitham, A. A. (2018). A cross sectional study about knowledge and practice of primigravida women: Minor and common pregnancy discomforts. *J Nurs Health Sci*, *4*(1), 32-45.

Bagot, C. N., Leishman, E., Onyiaodike, C. C., Jordan, F., Gibson, V. B., & Freeman, D. J. (2019). Changes in laboratory markers of thrombotic risk early in the first trimester of pregnancy may be linked to an increase in estradiol and progesterone. *Thrombosis research*, *178*, 47-53.

Bhowmik, B., Siddique, T., Majumder, A., Mdala, I., Hossain, I. A., Hassan, Z., ... & Hussain, A. (2019). Maternal BMI and nutritional status in early pregnancy and its impact on neonatal outcomes at birth in Bangladesh. *BMC pregnancy and childbirth*, *19*, 1-14.

Bohn, M. K., Nichols, M., Yang, L., Bhayana, V., Macri, J., & Adeli, K. (2023). Pediatric Reference Value Profiling of Essential Trace and Toxic Elements in Healthy Children and Adolescents Using High-Resolution and Triple Quadrupole Inductively Coupled Plasma Mass Spectrometry. *The Journal of Applied Laboratory Medicine*, *8*(4), 674-688.

Cabezuelo, M. T., Zaragozá, R., Barber, T., & Viña, J. R. (2019). Role of vitamin A in mammary gland development and lactation. *Nutrients*, *12*(1), 80.

Gilmore, J. H., Knickmeyer, R. C., & Gao, W. (2018). Imaging structural and functional brain development in early childhood. *Nature Reviews Neuroscience*, *19*(3), 123-137.

Godswill, A. G., Somtochukwu, I. V., Ikechukwu, A. O., & Kate, E. C. (2020). Health benefits of micronutrients (vitamins and minerals) and their associated deficiency diseases: A systematic review. *International Journal of Food Sciences*, *3*(1), 1-32.

Godswill, A. G., Somtochukwu, I. V., Ikechukwu, A. O., & Kate, E. C. (2020). Health benefits of micronutrients (vitamins and minerals) and their associated deficiency diseases: A systematic review. *International Journal of Food Sciences*, *3*(1), 1-32.

Grieger, J. A., Grzeskowiak, L. E., Smithers, L. G., Bianco-Miotto, T., Leemaqz, S. Y., Andraweera, P., ... & Roberts, C. T. (2019). Metabolic syndrome and time to pregnancy: a retrospective study of nulliparous women. *BJOG: An International Journal of Obstetrics & Gynaecology*, *126*(7), 852-862.

Jang, W., Kim, H., Lee, B. E., & Chang, N. (2018). Maternal fruit and vegetable or vitamin C consumption during pregnancy is associated with fetal growth and infant growth up to 6 months: results from the Korean Mothers and Children's Environmental Health (MOCEH) cohort study. *Nutrition journal*, *17*, 1-10.

Kavle, J. A., & Landry, M. (2018). Addressing barriers to maternal nutrition in low-and middle-income countries: A review of the evidence and programme implications. *Maternal & child nutrition*, *14*(1), e12508.

Mousa, A., Naqash, A., & Lim, S. (2019). Macronutrient and micronutrient intake during pregnancy: an overview of recent evidence. *Nutrients*, *11*(2), 443.

Oh, C., Keats, E. C., & Bhutta, Z. A. (2020). Vitamin and mineral supplementation during pregnancy on maternal, birth, child health and development outcomes in low-and middle-income countries: a systematic review and meta-analysis. *Nutrients*, *12*(2), 491.

Rafeeq, H., Ahmad, S., Tareen, M. B. K., Shahzad, K. A., Bashir, A., Jabeen, R., & Shehzadi, I. (2020). Biochemistry of fat soluble vitamins, sources, biochemical functions and toxicity. *Haya: The Saudi Journal of Life Sciences*, *5*(6), 188-196.

Rhodes, J. S., Rendeiro, C., Mun, J. G., Du, K., Thaman, P., Snyder, A., ... & Kuchan, M. J. (2020). Brain α-tocopherol concentration and stereoisomer profile alter hippocampal gene expression in weanling mice. *The Journal of Nutrition*, *150*(12), 3075-3085.

Shehan, J. N., Danis III, D. O. N., Bains, A., Basa, K., Marston, A. P., & Levi, J. R. (2021). Cleft palate in newborns diagnosed with prematurity. *Otolaryngology–Head and Neck Surgery*, *165*(6), 887-894.