

## **Effect of Vitamin A on Glucose Tolerance in Female Undergraduates of Ambrose Alli University, Ekpoma**

### **Abstracts**

**Background:** This study explored the effects of Vitamin A supplementation on glucose tolerance among female undergraduate students at Ambrose Alli University, Ekpoma, adopting a comprehensive metabolic approach. Recent evidence has established that retinoid signaling pathways interact with glucose metabolism through nuclear receptor networks, particularly through Retinoid X Receptor (RXR) pathways, which regulate insulin sensitivity and glucose homeostasis. **Objective:** The primary goals were to assess the influence of Vitamin A supplementation on fasting blood glucose levels and to evaluate its impact on glucose tolerance test results, specifically through the oral glucose tolerance test (OGTT), based on the molecular understanding of retinoid-mediated metabolic regulation. **Method:** The research involved conducting an OGTT on participants under two conditions: one without Vitamin A supplementation and another following a 100,000 IU dose of Vitamin A. Blood glucose levels were measured at six intervals (0, 30, 60, 90, 120, and 150 minutes) using an ACCU-CHEK Active glucometer, allowing for a detailed analysis of temporal glucose responses. Statistical analysis was carried out using a two-way ANOVA with GraphPad Prism 5 software to rigorously examine variations in glucose metabolism. **Result:** The results revealed subtle but statistically significant fluctuations in blood glucose levels across different time points. However, the data indicated that Vitamin A supplementation had minimal direct effects on glucose tolerance. While the study was limited by its sample size and generalizability, it provides valuable baseline data on the metabolic responses of young female adults. **Conclusion:** This research highlights the complex interplay between micronutrient supplementation and glucose metabolism. By investigating the effects of Vitamin A intake on glucose metabolism, the study addresses a critical gap in understanding the metabolic role of this essential micronutrient.

**Keywords:** Glucose, Vitamin A, Tolerance, Insulin, Resistance, Female, Nutrition intake oral

## **1. Introduction**

Vitamin A deficiency remains a pressing public health issue in many developing countries, with significant health implications. These range from severe conditions such as xerophthalmia, which can lead to blindness, to heightened susceptibility to infections and increased mortality rates (Sommer & West, 1996). Efforts to mitigate Vitamin A deficiency through supplementation or food fortification have demonstrated substantial benefits, including improved child survival rates (Beaton et al., 1993; Sommer & West, 1996).

The investigation of Vitamin A's effects on glucose metabolism is grounded in molecular evidence demonstrating retinoid involvement in metabolic regulation. Retinoid X Receptors (RXRs) form functional complexes with metabolic regulators such as Peroxisome Proliferator-Activated Receptors (PPARs), directly influencing glucose homeostasis and insulin sensitivity. Furthermore, retinoic acid signaling affects pancreatic  $\beta$ -cell function and insulin secretion through both genomic and non-genomic pathways. These established molecular mechanisms provide the theoretical basis for examining Vitamin A's potential impact on glucose metabolism, particularly in the context of supplementation.

Historically, clinical vitamin A deficiency has been linked to poor growth outcomes in children. Research has shown that the severity of eye conditions such as xerophthalmia correlates with stunting and wasting (Sommer, 1982). Children with mild forms of xerophthalmia, such as night blindness or Bitot's spots, often experience slower weight and height gains compared to their peers. While spontaneous recovery from xerophthalmia can sometimes lead to improved weight gain, the associated catch-up growth in height tends to be less pronounced (Tarwotjo et al., 1992). This raises questions about whether the growth effects are directly attributable to Vitamin A or influenced by other factors, such as overall nutritional status and disease burden, both of which also play critical roles in growth.

Studies investigating the effects of Vitamin A supplementation in non-xerophthalmic children have produced mixed results. While some research has reported positive impacts on weight or height gain, others have found little or no effect, leaving uncertainties about the specific role of Vitamin A in supporting growth (Fawzi et al., 1997; Lie et al., 1993; Rahmathullah et al., 1991; Ramakrishnan et al., 1995).

The Oral Glucose Tolerance Test (OGTT) is a widely used diagnostic tool to evaluate how efficiently the body processes glucose. During this test, a person consumes a measured quantity

of glucose, and blood sugar levels are monitored over time. Elevated glucose levels during an OGTT may indicate impaired glucose tolerance, a condition that can precede diabetes mellitus. Gestational diabetes, a condition characterized by elevated blood sugar levels during pregnancy due to hormonal changes, also relies on OGTT for diagnosis. Notably, blood sugar levels in gestational diabetes typically normalize postpartum (Balk et al., 2007).

## 2. Materials and Methods

UNDER PEER REVIEW

This study involved female undergraduate volunteers from Ambrose Alli University who were non-pregnant and not using anti-diabetic medications. Participants were randomly divided into two groups:

- **Vitamin A Supplemented Group:** Received a single dose of Vitamin A (100,000 IU).
- **Control Group:** Did not receive any Vitamin A supplementation.

### Measuring Instruments

The following instruments and materials were utilized:

- Measuring tape
- Stand meter
- Blood pressure apparatus (OMRON, M2 Basic, Automatic)
- Glucometer (ACCU-CHEK Active, Roche Diagnostic)
- Water (EVA, Nigeria Bottling Co. Ltd)
- Glucose (Fisher Scientific Co., USA)
- Vitamin A carotene (100,000 IU and 200,000 IU formulations)

### Oral Glucose Tolerance Test (OGTT) Protocol

- **Baseline Blood Sample:** A baseline blood sample was collected from each participant via finger prick.
- **Glucose Load:** Participants consumed 200 ml of a glucose solution containing 75 g of glucose within 5 minutes.
- **Blood Glucose Measurements:** Blood samples were subsequently collected via finger prick at six-time points: 0 (baseline), 30, 60, 90, 120, and 150 minutes.
- **Blood Glucose Analysis:** Blood glucose levels were measured at each time point using an ACCU-CHEK Active glucometer (Roche Diagnostic).

### Key Methodological Features

1. The study utilized a 75 g glucose solution for the OGTT.
2. Blood glucose levels were monitored over 150 minutes at intervals of 30 minutes.

3. Two experimental conditions were evaluated:
  - o Control group without Vitamin A supplementation.
  - o Experimental group with Vitamin A supplementation (100,000 IU).
4. Glucose measurements were performed with precision using the ACCU-CHEK Active glucometer.

UNDER PEER REVIEW

### 3. Analysis of Results

**Table 1:** Effect of Vitamin A on Glucose Tolerance ((mg/dL) in Female Undergraduate of Ambrose Alli University, Ekpoma

Post –Prandial Time (Min)	Changes in Blood Glucose (mg/dL)	Without Vitamin A With Vitamin A (100,000 IU)
0	63.74 ± 10.04 a	71.36 ± 10.13 a
30	102.7 ± 13.68 b	92.73 ± 13.68 a
60	112.91 ± 26.01 c	107.64 ± 17.77 a
90	98.18 ± 23.97 d	106.37 ± 21.37 a
120	98.18 ± 23.97 d	99.09 ± 17.33 a

150 85.73 ± 11.55 e 92.64 ± 16.09 a

*Values are expressed as mean ± SD (Standard Deviation): The values in the same rows with different alphabetic superscripts are considered significantly different (p < 0.05)*

The analysis revealed that the highest glucose level occurred at 120 minutes (2 hours) with a mean value of 98.18 mg/dL. Lower glucose levels were observed at the start of the test (0 minutes) with a mean of 63.74 mg/dL and at the end of the test (150 minutes) with a mean of 85.73 mg/dL. The 2-hour glucose level fell within the normal range for non-diabetic individuals, which is defined as below the standard 2-hour mean glucose tolerance test (GTT) value of 140 mg/dL.

#### Vitamin A Supplemented Group

In participants who received Vitamin A supplementation, the highest glucose level was recorded

at 1 hour (107.64 mg/dL), while the lowest level was observed at 0 minutes (71.36 mg/dL). Statistical analysis revealed no significant differences ( $p > 0.05$ ) in glucose levels between the 2-hour time point and other measured time points. Importantly, the 2-hour glucose level in this group also remained within the normal range for non-diabetic individuals, consistent with the standard 2-hour mean GTT value.

These findings indicate that glucose levels across time points in both groups were within normal limits, and the supplementation of Vitamin A did not significantly alter glucose tolerance.

UNDER PEER REVIEW

#### **4. Discussion**

Vitamin A, or retinol in mammals, is a fat-soluble vitamin essential for numerous physiological processes, including growth, tissue differentiation, and immune function. Humans acquire Vitamin A through two main dietary sources: pro-vitamin A (carotenoids) from plant-based foods like carrots, spinach, and sweet potatoes, and preformed Vitamin A (retinol) from animal-derived products such as liver, whole milk, fish oil, and eggs. Increased intake of Vitamin A, either through supplementation or food fortification, has been shown to significantly enhance child survival rates in regions with Vitamin A deficiency (Beaton et al., 1993; Sommer & West, 1996). The Oral Glucose Tolerance Test (OGTT) is a widely used diagnostic tool for evaluating the body's ability to regulate blood sugar levels. During the OGTT, a measured glucose load is consumed, and blood sugar levels are monitored at specific time intervals. Elevated blood sugar levels during the test may indicate impaired glucose tolerance, a precursor to diabetes mellitus or gestational diabetes (American Diabetes Association, 2014).

This study explored the effect of Vitamin A supplementation on glucose tolerance in female undergraduate students. The findings revealed no significant differences in glucose levels between participants who received Vitamin A supplementation and those who did not. Glucose levels remained within normal limits for non-diabetic individuals across all time points, indicating that Vitamin A supplementation did not influence glucose metabolism.

Although Vitamin A plays a vital role in various cellular and metabolic functions, its impact on glucose tolerance appears to be minimal, as demonstrated by this study. These findings suggest that Vitamin A supplementation is unlikely to play a significant role in diabetes prevention or management. However, the study provides valuable baseline data on glucose response patterns in young adult females, with detailed measurements taken at 30-minute intervals over 150 minutes. The dataset offers comprehensive insights into glucose tolerance among the study population, contributing to the broader understanding of Vitamin A's role in metabolic health. Future research with larger, more diverse populations and varying supplementation protocols could further

elucidate the relationship between Vitamin A and glucose metabolism.

## **5. Conclusion**

This study concluded that Vitamin A supplementation had no significant impact on glucose tolerance in female undergraduate students of Ambrose Alli University. After 2 hours of OGTT, glucose levels remained within the normal range for non-diabetic individuals, regardless of supplementation. These findings suggest that while Vitamin A is essential for various physiological functions, it does not substantially influence glucose metabolism or diabetes risk.

UNDER PEER REVIEW

## **Abbreviations**

OGTT: Oral Glucose Tolerance Test IU: International Units ANOVA: Analysis of Variance.

## **Disclaimer (Artificial intelligence)**

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models,

etc. have been used during the writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

- 1.
- 2.
- 3.

## **References**

American Diabetes Association. (2014). Standards of Medical Care in Diabetes--2014. *Diabetes Care*. 37(1): 14-80.

Amini, M. and Janghorbani, M. (2007). Diabetes and Impaired Glucose Regulation in First-Degree Relatives of Patients with Type 2 Diabetes in Isfahan, Iran: Prevalence and Risk Factors. *Review of Diabetic Studies*. 4:169–176.

Antuna-Puente, B., Disse, E., Rabasa-Lhoret, R., Laville, M., Capeau, J. and Bastard, J. P. (2011). How can we Measure Insulin Sensitivity/Resistance? *Diabetes and Metabolism*. 37(5): 179–188.

Balk, E. M., Tatsioni, A., and Lichtenstein, A. H. (2007). Effect of Chromium Supplementation on Glucose Metabolism and Lipids: A Systematic Review of Randomized Controlled Trials. *Diabetes Care*. 30: 2154-2163.

Beaton, G.- H., Martorell, R., Aronson, K. J., Edmonston, B., McCabe, G., Ross, A. C. And Harvey, B. (1993). Effectiveness of Vitamin A Supplementation in the Control of Young Child Morbidity and Mortality in Developing Countries. ACC/SCN State of the Art Series Nutrition Policy Discussion Paper, No. 13.

Brazis, P. W. (2004). Pseudotumor cerebri. *Current Neurology and Neuroscience Reports*.4(2): 111-116.

Brown, D. C., Byrne, C. D., Clark, P. M., Cox, B. D., Day, N. E., Hales, C. N., Shackleton, J. R., Wang, T. W. and Williams, D. R. (1991). Height and Glucose Tolerance in Adult Subjects. *Diabetologia*. 34(7):531–533.

Conn, J. W. (1990). Interpretation of the Glucose Tolerance Test. The Necessity of a Standard Preparatory Diet. *American Journal Medical Sciences*. 199: 555–164.

DeFronzo, R. A. and Abdul-Ghani, M. (2011). Assessment and Treatment of Cardiovascular Risk in Prediabetes: Impaired Glucose Tolerance and Impaired Fasting Glucose. *American Journal of Cardiology*. 108: 3–24

Duester, G. (2008). Retinoic Acid Synthesis and Signaling during Early Organogenesis. *Cell*. 134(6): 921–931.

Fawzi, W. W., Herrera, M. G., Willett, W. C., Nestel, P., El Amin, A. and Mohamed, K. A. (1997). Vitamin A Supplementation Does not Improve Growth of Preschool Children in the Sudan. *American Journal of Public Health*. 12: 34-45.

Fuchs, E. and Green, H. (1991). Regulation of Terminal Differentiation of Cultured Human Keratinocytes by Vitamin A. *Cell*. 25(3): 617–625.

Furr, H. C., Amedee-Manesme, O. and Clifford, A. J. (1999). Vitamin A Concentrations in Liver Determined by Isotope Dilution Assay with Tetradeuterated Vitamin A and By Biopsy in Generally Healthy Adult Humans. *American Journal of Clinical Nutrition*. 49: 713-716.

UNDER PEER REVIEW

Gudas, L. J. and Wagner, J. A. (2011). Retinoids Regulate Stem Cell Differentiation. *Journal of Cell Physiology*. 226: 322–330.

Lie, C., Ying, C., En-Lin, W., Brun, T. and Geissler, C. (1993). Impact of Large-Dose Vitamin A Supplementation on Childhood Diarrhoea, Respiratory Disease and Growth. *European Journal of Clinical Nutrition*. 47: 88-96.

Lin, S. H., Yang, Z., Liu, H. D., Tang, L. H. and Cai, Z. W. (2011). Beyond Glucose: Metabolic



Shifts in Responses to the Effects of the Oral Glucose Tolerance Test and the High-Fructose Diet in Rats. *Molecular BioSystems*. 7:1537-1548.

Mohsen, J. and Massoud, A. (2008). Effects of Gender and Height on the Oral Glucose Tolerance Test: The Isfahan Diabetes Prevention Study. *Journal of the Society for Diabetes Research*. 5(3): 163–170.

Muniyappa, R., Lee, S., Chen, H. and Quon, M. J. (2008). Current Approaches for Assessing Insulin Sensitivity and Resistance In Vivo: Advantages, Limitations, and Appropriate Usage. *American Journal of Physiology, Endocrinology and Metabolism*. 294 (1): 15–26.

Olson, J. A. (1994). Hypovitaminosis A: Contemporary Scientific Issues. *Journal of Nutrition*. 124: 1461–1466.

Palczewski, K. (2012). Chemistry and Biology of Vision. *Journal of Biological Chemistry*. 287: 1612–1619.

Pellis, L., van Erk, M. J., van Ommen, B., Bakker, G. C. M. and Hendriks, H. F. J. (2012). Plasma Metabolomics and Proteomics Profiling after a Postprandial Challenge Reveal Subtle Diet Effects on Human Metabolic Status. *Metabolomics*. 8:347-359.

Rahmathullah, L., Underwood, B. A., Thulasiraj, R. D. and Milton, R. C. (1991). Diarrhea, Respiratory Infections, and Growth are not Affected by A Weekly Low-Dose Vitamin A Supplement: A Masked, Controlled Field Trial in Children in Southern India. *American Journal of Clinical Nutrition*. 54: 568-577.

Ramakrishnan, U., Latham, M. C. and Abel, R. (1995). Vitamin A Supplementation Does not Improve Growth of Preschool Children: A Double-Blind Field Trial in Southern India. *Journal of Nutrition*. 125: 202-21131

Schulz, C., Engel, U., Kreienberg, R. and Biesalski, H. K. (2007). Vitamin A and Beta-Carotene Supply of Women with Gemini or Short Birth Intervals: A Pilot Study. *European Journal of Nutrition*. 46(1): 12–20.

Sicree, R. A., Zimmet, P. Z., Dunstan, D. W., Cameron, A. J., Welborn, T. A. and Shaw, J. E. (2008). Differences in Height Explain Gender Differences in the Response to the Oral Glucose Tolerance Test. *Diabetic Medicine*. 25(3): 296–302.

Sommer, A. (1982). *Nutritional Blindness, Xerophthalmia, and Keratomalacia*. Oxford University Press, New York. Pp. 107–122.

Sommer, A. and West, K. P. (1996). *Vitamin A Deficiency*. In: *Health, Survival and Vision*. Oxford University Press, New York. Pp. 19–250.

UNDER PEER REVIEW

Tang, G., Qin, J., Dolnikowski, G. G., Russell, R. M. and Grusak, M. A. (2005). Spinach Carrots can supply significant amounts of vitamin A as assessed by feeding them with intrinsically deuterated vegetables. *The American Journal of Clinical Nutrition*. 82(4): 821–828.

Tanumihardjo, S. A (2011). *Vitamin A: Biomarkers of Nutrition for Development*. *The American Journal of Clinical Nutrition*. 94(2): 658–665.

- Tarwotjo, I., Katz, J., West, K. P., Tielsch, J. M. and Sommer, A. (1992). Xerophthalmia and Growth in Preschool Indonesian Children. *American Journal of Clinical Nutrition*. 55:1142-1146.
- Unwin, N., Shaw, J., Zimmet, P. and Alberti, K. G. (2002). Impaired Glucose Tolerance and Impaired Fasting Glycaemia: The Current Status on Definition and Intervention. *Diabetic Medicine*. 19:708–723.
- Villamor, E. and Fawzi, W. W. (2005). Effects of Vitamin A Supplementation on Immune Responses and Correlation with Clinical Outcomes. *Clinical Microbiology Review*. 18(3): 446–464.
- Villamor, E. and Fawzi, W. W. (2005). Effects of Vitamin A Supplementation on Immune Responses and Correlation with Clinical Outcomes. *Clinical Microbiology Reviews*. 18(3): 446-464.
- Wolf, G. (2001). The Discovery of the Visual Function of Vitamin A. *The Journal of Nutrition*. 131(6): 1647–1650.
- Zhao, X. J., Peter, A., Fritsche, J., Elcnerova, M. and Fritsche, A. (2009). Changes of the Plasma Metabolome during an Oral Glucose Tolerance Test: Is There More Than Glucose To Look At? *American Journal of Physiology: Endocrinology and Metabolism*. 296: 384-393.
- Esteban-Pretel, G., et al. (2021). "Vitamin A and Retinoid Signaling in the Regulation of Glucose and Energy Metabolism." *Nutrients*, 13(5): 1456.
- Li, Y., et al. (2022). "Nuclear Receptor Signaling in Metabolic Regulation: The Role of Vitamin A." *Cell Metabolism*, 34(3): 322-337.
- Wang, B., et al. (2023). "Retinoid X Receptor-Mediated Metabolic Control: Implications for Glucose Homeostasis." *Molecular Metabolism*, 68: 101559.
- Zhang, R., et al. (2023). "Vitamin A-Dependent Transcriptional Networks in Metabolic Regulation." *Nature Reviews Endocrinology*, 19(2): 78-92.